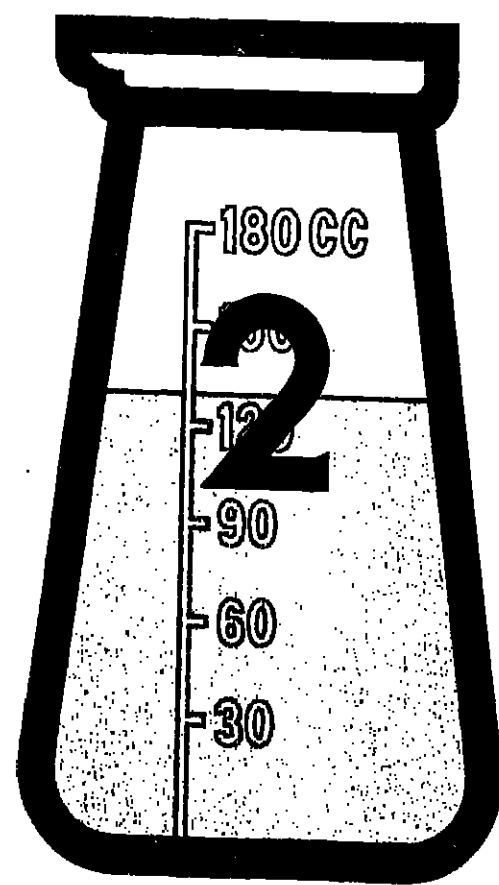


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Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms.

Notes: Carefully coordinate in vitro sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical

signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma, in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); allergic reactions (pyrexia, multi-forme, skin eruptions, epidermal necrolysis, urticaria, rash, skin eruptions, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); CNS reactions (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); miscellaneous reactions (drug fever, chills, toxic nephrosis with oliguria and anuria, periarthritis nodosa and E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis). Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm b.i.d. or t.i.d. depending on severity of infection. Usual child's dosage: 0.5 Gm (1 tab or teasp.) / 20 lbs of body weight initially, then 0.25 Gm / 20 lbs b.i.d. Maximum dose should not exceed 75 mg / kg / 24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole / teaspoonful.

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world news of medicine and its practice—fast, accurate, complete

and Medical News

Wednesday, July 23, 1975

'Double Trouble' Theory Glucagon Role In Diabetes Is Expounded

By FRANCES GOODNIGHT
Medical Tribune Staff

NEW YORK—The new "double trouble" hypothesis of diabetes and its implications for changes in patient treatment were assessed here by Dr. Roger H. Unger, of Southwestern Medical School, whose work has been crucial to the concept of diabetes as a hormonal abnormality—glucagon excess as well as insulin deficiency.

The complex issue of the relationship of the alpha-cell and beta-cell abnormality in inherited human diabetes is still unsettled, Dr. Unger said in the Banting Memorial Lecture at the annual meeting of the American Diabetes Association.

What has been definitely established, in his view, is that the quantities of exogenous insulin required to reduce the hyperglucagonemia in human diabetes exceed the amounts secreted in normal people; and that glucagon suppression by somatostatin "can achieve a level of glucoregulation with only a fraction of the insulin dose otherwise required."

Citing recent studies in juvenile diabetes, Dr. Unger noted that glucagon

Continued on page 2

Convention Impressions by Ida Libby Dengrove



Ida Libby Dengrove, a doctor's wife who is a noted TV artist, again draws her impressions of an A.M.A. convention. See pages 12-13.

Stanford Estimate:

Up to 3,100,000 Have Ankylosing Spondylitis in US

Medical Tribune Report

NEW ORLEANS—As many as 3,100,000 Americans may have undiagnosed ankylosing spondylitis, Stanford University rheumatologists believe.

A study further suggests that the disease is nearly as common among women as men, in contradiction to the presently-accepted ratio of 1 to 10.

Continued on page 16

making rounds at press time

PUBLIC CONFIDENCE in doctors is plummeting, according to a new Harris poll. Though M.D.s still rated the most honest group, only 45% of Americans now have a "great deal" of confidence in them, compared with 72% in 1966. "High confidence" was given by 51% to garbage men, since "at least we know whether or not they take away the trash."

Moderate View On PSROs Wins At AMA Parley

By EDWARD GROSSMAN
Medical Tribune Staff

ATLANTIC CITY, N.J.—Some delegates at the American Medical Association annual meeting here, encouraged by a recent federal court decision that enjoined the Department of Health, Education, and Welfare from implementing certain provisions of the Professional Standards Review Organizations law, urged the A.M.A. to support physicians who refuse to cooperate with governmental review procedures, and come out for complete repeal of P.S.R.O.

But other delegates cautioned against such actions, saying it would be best for the A.M.A. to stick with its policy, enunciated last year, of advising members to cooperate with the government while keeping control of review boards in the hands of local physicians and working for amendments to the law.

In voting on a variety of resolutions concerning mandatory P.S.R.O. and voluntary peer review, it was generally the moderate view that prevailed.

The federal court decision on a suit of the A.M.A. against H.E.W., handed down by Judge Julius J. Hoffman in Chicago on May 27, granted an injunction forbidding participation of non-physicians in hospital utilization review

Continued on page 16

After 'Birth Without Violence,' Does a Baby Smile?



"Birth without violence" produces an infant who can smile on the first day of life, as Dr. Leboyer illustrates by gentle head-stroking.

By MICHAEL HERRING
Medical Tribune Staff

NEW YORK—Can a baby smile on the first day of life? Child psychologists say so. Dr. Ervin S. Nichols, director

of practice activities for the American College of Obstetrics and Gynecology, says, "I don't know. What's a smile? I'm not sure I can define a smile in a newborn."



Dr. Leboyer immediately gives the infant a lukewarm bath, reminiscent of uterine environment from which it has just emerged.

However, Dr. Frederick Leboyer thinks infants can smile, and showed them doing it in a film at Hunter College Auditorium, where he discussed his method of "Birth without violence."

The French pediatrician said he began trying to alleviate the trauma of birth eight years ago, when, he said, he realized that the baby is not an object

Continued on page 22

'Double Trouble' Diabetes Theory Expounded

Continued from page 1

suppression with somatostatin results in marked improvement in hyperglycemia without the massive doses of insulin otherwise needed, and even blocks the postprandial hyperglycemia these patients would usually experience.

"One cannot help but be impressed," he added, "with the potential therapeutic efficiency that a safe and practical glucagon-suppressing drug might offer in the control of diabetic hyperglycemia."

How immediate are the prospects for such clinical application?

Dr. Unger believes it would be "the height of irresponsibility" to suggest at the present time that safe therapy aimed at correction of both of the double troubles of hyperglucagonemia and hypoinsulinemia would offer more than conventional methods of glucoregulation directed solely at insulin delivery.

"But it would be the height of nihilism not to hope, and the height of indifference not to find out," he emphasized.

During his lecture, Dr. Unger—introduced affectionately as "Mr. Glucagon"—outlined the following description of the glucoregulatory functions of glucagon and insulin:

The unique biologic opposition of the two hormones endows the alpha-cell, beta-cell unit with the ability to vary glucose flux in a manner physiologically appropriate to prevailing circumstances while maintaining extracellular glucose concentrations within "remarkably narrow limits," irrespective of those circumstances.

Insulin is the hormone of glucose efflux from the extracellular space and glucagon normally acts as the dominant regulator of glucose influx even though insulin also restrains glucose influx.

Influx and Efflux

If the concentration of glucose in extracellular fluid is to remain unchanged when glucose flux changes, it is obvious that the influx and efflux must remain equal. At the time of violent exercise, for example, the efflux into muscle rises and the influx must increase proportionately to keep glucose concentration constant. This takes place, partly under the influence of a marked increase in glucagon, with the result that hypoglycemia is prevented and the central nervous system is assured of enough glucose.

Conversely, food intake increases exogenous glucose influx and glucose efflux must increase proportionately if hyperglycemia is to be avoided. This is achieved by a rise in insulin secretion.

Dr. Unger pointed out that such neat balancing continues throughout the lifetime of the normal, healthy person. The extracellular fluid glucose concentration stays within narrow limits except when critical injury or other serious stress demands an increase to maintain cerebral glucose delivery, and then nature's control system turns down insulin secretion and turns up glucagon secretion to maintain stress hyperglycemia as long as the threat persists.

The "double trouble" hypothesis of

diabetes, he said, "assigns to pancreatic and/or extrapancreatic glucagon the role of co-mediator of the full disorder" in carbohydrate metabolism.

According to this concept, insulin deficiency accounts for the underutilization of glucose but glucagon excess—relative or absolute—causes most of the glucose overproduction.

Whether diabetic hyperglucagonemia is suppressible by insulin is a question that cannot yet be answered definitively, Dr. Unger commented. Is there more than one type of diabetic hyperglucagonemia? Or could it be that—as in the case of dogs with alloxan diabetes—"the hyperglucagonemia derived from the gastrointestinal tract during underinsulation responds to insulin, while hyperglucagonemia of pancreatic origin is insulin-insensitive?"

Explanation Offered

But it is clear, he said, that most overt diabetics have a "double trouble," and that in most young juvenile-type diabetics the basal hyperglucagonemia is only partially corrected by high insulin doses. In others, insulin in extremely high doses is ineffective.

One explanation could be that the massive doses of insulin may be causing a high rate of glucose efflux "without sufficient sustained suppression of glucose influx during meals." And in-

appropriate mealtime hyperglucagonemia with a fixed level of circulating exogenous insulin "may be causing bursts of hyperglycemia."

Dr. Unger posed yet another question: "Is there an intrinsic defect affecting both the beta-cell and the alpha-cell, both of which originate from a common anlage?" The fact that diabetic alpha-cell secretion can be reduced by insulin, he cautioned, does not necessarily signify that its alpha-cell hyperactivity is secondary to insulin lack.

Biotheologic Inference

Although the investigator said that the possible long-term benefits of sustained metabolic normalization of the diabetic cannot be predicted by scientific evidence now available, he offered what he called "biotheologic inference" as a basis for guessing:

- "Nature's efforts are seldom purposeless."

- "Nature, through the coordinated secretion of insulin and glucagon, makes a formidable, and in most humans a remarkably successful, effort to avoid hyperglycemia throughout life."

- "These humans virtually always escape microangiopathy, whereas those humans in whom nature fails in its efforts to avoid hyperglycemia usually develop microangiopathy."

Computer-Simulated Pulsed Arterial Flow

Investigations by Johns Hopkins Applied Physics Laboratory scientists on complex and little-understood patterns of pulsing fluid flow in modeled arterial branches are shedding new light on the role of hemodynamics in developing arterial malfunctions and atherosclerosis. Here, a momentarily frozen-in-time view of the computer-simulated pulsed arterial flow in a symmetric bifurcation is revealed by a velocity vector field (where small lines represent magnitude and direction of local flow). At junction inlet, the flow is not distributed evenly in the channel; some of the flow is even at a virtual standstill (represented by the lack of velocity lines shown by small dots). At the centerline of the channel, the flow is stronger, but it diminishes as one goes downstream.

WHO Deplores Growing Traffic in Plasma

Medical Tribune World Service

GENEVA—Delegates from more than 130 countries attending the World Health Assembly here have been alerted to the disadvantages of a growing traffic in plasma originating in developing countries.

The traffic, which carries health risks for both donors and recipients of plasma substances, was described in a document issued to the meeting by the W.H.O. director-general, Dr. Halfdan Mahler.

The practice, which was first noted

by the League of Red Cross Societies, originated about 10 years ago in Central and South America and has recently spread to Asia and Africa.

Financially, it shows attractions for the unscrupulous, the report said. In some of the economically poorer countries, a liter of plasma may be bought from a donor for about \$1 or \$2, compared with a cost of \$20-40 in developed countries.

"In some centers now being operated, single or double plasmapheresis may be repeated up to several times

Saudi Arabia Opens Doors Wide to MDs

Medical Tribune World Service

GENEVA—With about \$14 billion to spend on health care development during the next five-year plan, Saudi Arabia is opening the doors wide to U.S. and European physicians.

"We estimate that we will need about half a million people, including doctors, nursing staff, and health technicians, to bring our medical system to the level we have planned," Dr. Samer Islam, director of regional health services and hospitals, Riyadh, said.

Dr. Islam, here to attend the World Health Assembly, pointed out that Saudi Arabia is at present one of the countries where native-born physicians are in the minority. There is heavy reliance on U.S. and European medical staff in the cities, particularly in government hospitals, while in the provinces most of the doctors are Arabic-speaking Muslims from Syria, Egypt, and Pakistan.

100 New Hospitals Planned

"We plan to build 100 hospitals over the next five years," Dr. Islam said. "Even if we achieve only half that target, we are still facing an enormous problem of staffing."

With the treasury awash with petrodollars, Saudi Arabian salary levels are likely to be competitive with U.S. rates. In government service, a medical officer gets roughly \$1,000 a month basic salary, plus a further \$800-\$1,000 compensation allowance for his estimated loss of earnings away from private practice. Other allowances include housing, education grants, and paid home leave.

Saudi Arabia's first medical school, which is under the sponsorship of London University School of Medicine, opened in Riyadh three years ago. A second, sponsored by Johns Hopkins University, is scheduled to open soon in Jidda, and a third school later. The three together are expected to graduate no more than 100 physicians a year when they are in full operation.

"So we are interested in getting U.S. and Europeans to set up also in private practice in our country," Dr. Islam told MEDICAL TRIBUNE.

Any doctor who wants to set up his own clinic or private hospital can probably qualify for a 50 per cent loan free of interest and spread over 10-15 years, he added.

per week on the same donor," Dr. Mahler said.

In undernourished plasma donors especially, this may result in a deficiency of proteins or other essential plasma components, impair the body's immune defenses, and provoke iron deficiency and anemia, it was noted.

For the recipients of at least some of the plasma derivatives, it has been established that there is a higher risk of contracting diseases, particularly hepatitis, when the plasma is from a paid source, the report said.

Chemonucleolysis for Disk Disease—Pros and Cons

Medical Tribune Report

SAN FRANCISCO—Two separate studies of chemonucleolysis for the treatment of discogenic back pain indicated that it has something to offer, but also that it could produce complications and poor results on a large scale.

The properly selected failed laminectomy patient can approach chemonucleolysis feeling he has "everything to gain and nothing to lose," Dr. Henry W. Apfelbach told the American Academy of Orthopaedic Surgeons. He is attending orthopaedic surgeon at Lake Forest Hospital in Lake Forest, Illinois.

Chemonucleolysis for disk disease is so easy and takes so little time "it could be improperly used or so widely and indiscriminately used as to produce a horrendous number of complications and poor results," Dr. Brian H. Huncke told the Academy.

'Controversies' Noted

Dr. Huncke took note of the "controversies" of chemonucleolysis and the question of F.D.A. approval before concluding that "chymopapain chemonucleolysis is a safe method for managing patients with discogenic back and leg pain." Dr. Huncke is Clinical Assistant Professor of Orthopaedic Surgery at Rush Medical School in Chicago.

Chemonucleolysis produces its best results in "patients who have back pain with unilateral sciatica with positive stretch tests," Dr. Huncke said.

Of his nearly 600 patients seen over three years, 47.4 per cent were male, 52.6 per cent female; 85.5 per cent of the patients were in good health with no associated orthopaedic diagnoses.

Dr. Apfelbach, in a separate study, concluded that "chemonucleolysis will give a high percentage of satisfactory results in the patient with a failed laminectomy."

He said that in 49 failed laminectomy patients given chymopapain injections for six months or more, results

were "excellent" in 24 patients, "good" in 10, "fair" in seven, and "poor" in nine.

"[Chemonucleolysis] appears to be especially useful in those patients who obtain a good result following their initial laminectomy for one year or more," Dr. Apfelbach said. "This group of patients appears to have a prognosis following chemonucleolysis similar to that of the patient with a herniated disc in a 'virgin' back."

Dr. Apfelbach added that the use of chemonucleolysis avoids open surgery and its accompanying high morbidity.

Previous Surgery

Dr. Huncke said his group's experience with patients who had previously undergone surgery "is quite similar to that of Dr. Apfelbach."

"Previous surgery, if productive of 12 or more months of relief for a patient—followed by a recurrence—does not contraindicate chemonucleolysis," Dr. Huncke said. "Previous surgery, if not productive of any relief at all, usually precludes success with chemonucleolysis."

Dr. Huncke said the taking of a de-

tailed and thorough history is the most critical element of patient selection, and that if patients are carefully selected, medico-legal and compensation problems are not significant.

Whether a patient has had previous surgery or not, Dr. Huncke said, any evidence of perineural, epidural or intradural scarring "mitigates against chemonucleolysis."

Myelography Used

Dr. Huncke said his group used myelography particularly to rule out arachnoiditis and other forms of scarring. Electromyography was used to detect possible polyneuritis. He called discography "an essential part of the procedure."

But Dr. Huncke warned, "Unless you can obtain valid and reliable electro-diagnostic studies, they are probably worse than useless."

Dr. Apfelbach said his group felt that if myelography had been done in the patients who failed to benefit from chemonucleolysis, it would probably have substantiated a diagnosis of arachnoiditis in some of them.

75% of Arthritics Held Capable of Satisfactory Sex Life

Medical Tribune Report

NEW ORLEANS—Three-fourths of all patients with rheumatoid arthritis are capable of leading satisfactory sex lives, the American Rheumatism Association meeting was told here, and physicians were urged to explain to them how they can do so.

If a practitioner feels uncomfortable in discussing the subject, he should refer the arthritic man or woman for counselling.

These points were made by Richard Rogal, Ph.D., of the Ruchos Los Amigos Hospital in Los Angeles.

Arthritis, he said, "have the same need to be loved physically and emotionally as the rest of humanity."

"There is a temptation for the practitioner who is uncomfortable about discussing sex just to hand out the pamphlets," Dr. Rogal said. More guidance is required, he emphasized.

He said only about one-fourth of arthritis patients have physical incapacities severe enough to rule out sexual acts completely. The others should be advised as to how they can perform satisfactorily despite their handicaps.

"Patients with sex problems often question their value as mates, mothers, fathers, breadwinners, and homemakers," he continued. "Young people are especially vulnerable. They start to wonder whether anybody ever will love them the way they are."

House Witnesses Clash on Federal Role in Malpractice Crisis

Medical Tribune Report

NEW YORK—Should the Federal Government intervene in the "malpractice crisis" that has now hit virtually every state in the union?

Recent hearings held here by the House Subcommittee on Health and the Environment, chaired by Representative Paul G. Rogers (D-Fla.), got a different answer from almost every witness, so the group indicated it will continue to weigh the question as it gathers more evidence and calls on other concerned parties.

As one witness, Gary Turndorf of the New Jersey State Society of Anesthetists, put it, the problem is clearly "local in nature, but national in scope," and the committee must go much further in investigating key issues before reaching a decision, according to Rep. Rogers.

Still unresolved is the questionable activity of the Argonaut Insurance Company, which "infected the entire state with the whole mess," according to Alfred Julien, who represented the New York Trial Lawyers Association. Indeed, the testimony of Lawrence

C. Baker, newly appointed president of the company that until July 1 insured some 30,000 New York doctors, was full of surprising disclosures. Mr. Baker testified that, while Argonaut took in \$35,000,000 in premiums last year, only \$24,000 has been paid out in claims since the company came to the state in 1974.

He added that the company would lose an additional \$69,000,000 associated with claims over the next 20 years, but, he said, Argonaut is responsible for only 54 per cent of that sum, or about \$37,000,000.

Because he became president of Argonaut only a few weeks before the hearing and joined the company in January, Mr. Baker could not answer questions about Argonaut's reasons for entering and leaving the state so abruptly, nor could he explain why the company recently rescinded its proposed 300 per cent rate increase rather than show its books to the State Insurance Department.

To learn more about the workings of Argonaut, Rep. Rogers indicated that he would call other members of

the Teletype Financial Corporation, a California conglomerate that owns the company, to testify at a later date.

In his testimony earlier in the day, Dr. Ivan L. Bennett, President of the New York County Medical Society, told the committee, "We have to do something to discourage the needless tests and x-rays that doctors are performing to defend themselves from patients. At the same time, we have to create an atmosphere in which new and innovative approaches to treatment can be tried, even though they might fail."

In addition, Dr. Robert Hicks, testifying for the New York State Medical Society, pointed out the irony of the situation: "It isn't the uneducated or elderly physician that suffers most from malpractice claims," he said, "but the highly exposed, outstanding specialist, who often sees patients in the worst condition."

The majority of such claims, he added, are not based on negligence, but on a poor result or technical difficulty from a procedure that disappointed the patient.

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CLINICAL NEWS NOTE: "When you look at your bank account, you look at the bottom line, and I think that's what we have to do with this [Leboyer 'birth without trauma' procedure] thing. If in fact Leboyer can show 100,000 deliveries this way with better results, then I think there's nothing we can do but to take a real solid look at it." (Dr. Ervin E. Nichols, see page 22.)

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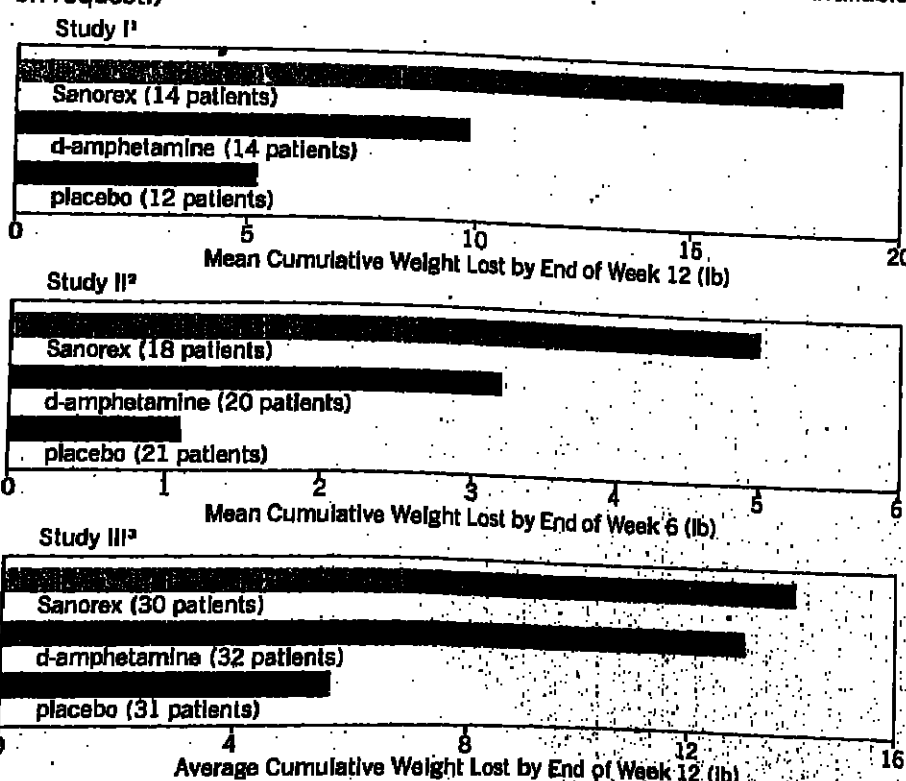
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Different Neurochemical Action*

Animal studies suggest that Sanorex, unlike d-amphetamine, does not interfere with norepinephrine synthesis. In animal studies, d-amphetamine (like food) activates afferent neurons leading to appetite centers in the hypothalamus. Resulting release of norepinephrine activates the receptor neurons. Unlike food, however, d-amphetamine also suppresses norepinephrine synthesis. Thus, increasingly larger doses of d-amphetamine become necessary to produce an effect.

Action of Sanorex: After intake of food stimulates the release of norepinephrine from afferent neurons, Sanorex blocks its re-uptake without disturbing normal synthesis and release.

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Simple one-a-day dosage is facilitated by 2-mg tablets (taken one hour before lunch). New flexibility (for the patient in whom 1 mg t.i.d. is preferred) is now facilitated by new 1-mg tablets (taken one hour before meals).

*The significance of these differences for humans is uncertain.

For Brief Summary, please see facing page.

Wednesday, July 23, 1975

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3. Varrone EJ: Practical considerations for managing obese patients: initial interview and follow-up treatment in the office. Scientific Exhibit presented at the American Medical Association, 27th Clinical Convention, Anaheim, Calif., Dec 1-4, 1973.

Indication: In exogenous obesity, as a short-term (a few weeks) adjunct in a weight-reduction regimen based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors.

Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crisis may result).

Warnings: Tolerance to many anorectic drugs may develop within a few weeks; if this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Interactions: May decrease the hypotensive effect of guanethidine; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines; if a patient recently taking mazindol must be given pressor amine agents (e.g., levaterenol or isoproterenol) for shock (e.g., from a myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and initiating pressor therapy with a low initial dose and careful titration.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulant drugs that have been extensively abused and can produce tolerance and severe psychological dependence. Manifestations of chronic overdosage, or withdrawal with mazindol have not been determined in humans. Abstinence effects have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Use in Pregnancy: In rats and rabbits an increase in neonatal mortality and a possible increased incidence of rib anomalies in rats were observed at relatively high doses. Although these studies have not indicated important adverse effects, the use of mazindol in pregnancy or in women who may become pregnant requires that potential benefit be weighed against possible hazard to mother and infant.

Use in Children: Not recommended for use in children under 12 years of age.

Precautions: Insulin requirements in diabetes mellitus may be altered. Smallest amount of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdosage. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.

Adverse Reactions: Most commonly, dry mouth, tachycardia, constipation, nervousness, and insomnia. Cardiovascular: Palpitation, tachycardia. Central Nervous System: Overstimulation, restlessness, dizziness, insomnia, dysphoria, tremor, headache, depression, drowsiness, weakness. Gastrointestinal: Dryness of mouth, unpleasant taste, diarrhea, constipation, nausea, other gastrointestinal disturbances. Skin: Rash, excessive sweating, changes in libido have rarely been observed. Eye: Long-term treatment with high doses in dogs resulted in some corneal opacities; reversible on cessation of medication; no such effect has been observed in humans.

Dosage and Administration: 1 mg three times daily, one hour before meals, or 2 mg per day, taken one hour before lunch in a single dose.

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MEDICAL TRIBUNE

5

Current Opinion

'Genetic Engineering' and the Role of the Public

Part II

What relations between biomedical scientists and the public should be concerning research was the focus of Dr. Stanley N. Cohen's recent testimony on "genetic engineering" before the Senate Subcommittee on Health. Dr. Cohen, Associate Professor of Medicine at Stanford University Medical Center, was one of the medical scientists who developed the procedure by which the hereditary characteristics of almost any kind of animal or plant cell could be introduced into bacteria. Because this issue—as well as the scientific work itself—has profound implications for medicine and physicians, MEDICAL TRIBUNE is publishing a condensation of Dr. Cohen's testimony.

AT ASILOMAR MEETING, discussions of experimental safety were again carried out under full public scrutiny. One of every eight attendees at the conference was a representative of the press; many reporters recorded the formal sessions of the meeting on tape, and in addition, spent the evenings at Asilomar asking the scientist participants relevant, pointed, and challenging questions with a journalistic intensity.

Also participating actively in the discussions and decisions of Asilomar were representatives of the National Science Foundation and the National Institutes of Health, as well as invited non-scientists from the fields of law and ethics. Following the Asilomar conference, a public meeting of the newly appointed NIH Advisory Committee on Recombinant DNA Molecules was again attended by representatives of the national press, and at that session, formal action was taken to add a permanent non-scientist member to the scientific group advising the federal government in this area.

Consensus on Issues

There was a general consensus among the participants at Asilomar on three major issues:

1) Genetic manipulation of bacteria and viruses offers the prospect for solution of a wide variety of important scientific and medical problems, as well as other problems that plague society—such as environmental pollution, and food and energy shortages.

2) The participants agreed that accidental dissemination of certain kinds of genetically altered bacteria and viruses may pose varying degrees of potential risk. Thus, the scientists proposed a series of safeguards, principally biological and physical barriers, adequate to allow most experiments to be undertaken with minimal risk to laboratory workers, to the public at large, and to the animal and plant species sharing our ecosystems.

3) The participants at the conference concluded that there are certain experiments in which the potential risks are of such a serious nature that they ought not be done with the present

"... participants ... concluded that there are certain experiments in which the potential risks are of such a serious nature that they ought not to be done with the presently available containment facilities ..."

ently available containment facilities. This determination was based simply on a judgment of potential risk; it did not involve decisions about the scientific merit of the experiments, or judgments about their usefulness. It was agreed that standards of protection should be greater at the beginning and should be modified as the assessment of risk changes.

Physical containment barriers have

long been used in the United States space exploration program to minimize the possibility of contamination of this planet by extra-terrestrial microbes. Such procedures have also been employed to protect laboratory workers and the public from hazards associated with the use of radioactive materials and toxic chemicals, and with the study of disease-causing bacteria and viruses.

The concept of biological barriers, which was formulated in some detail at Asilomar, and which involves fastidious bacterial hosts unable to survive in

"... The concept of biological barriers ... will contribute significant additional safety to gene manipulation experiments."

natural environments and equally fastidious vehicles able to grow only in specified hosts, will contribute significant additional safety to gene manipulation experiments.

Model: Radioactivity

The procedures developed for work with radioactive materials provide a useful model for other types of potentially biohazardous experiments; radioisotope use is subject to regulations designed to ensure the safety of laboratory personnel and the general public, and there is public involvement in the enforcement of these safety procedures. However, the merit or lack of merit of specific experiments that employ radioactive materials is entirely a scientific judgment that is determined by the peer review system.

Moreover, the public does not require that a scientist seeking to use radioactive materials in the search for basic scientific knowledge justify the use of this experimental tool in terms of the public benefits to be obtained from particular experiments.

Details of the mechanisms now being developed to monitor potentially biohazardous experimentation in the area of bacterial and viral gene manipulation have not yet been announced. However, it has been proposed that the extent of risk of experiments be determined by the current peer review process; the appropriate containment conditions required for particular experiments would be specified by the same mechanism. Furthermore, on-site inspection of containment facilities by local biohazards committees would determine whether the required safety precautions are being implemented.

properly. Under such conditions of containment, studies designed to assess more accurately the actual extent of risk for various types of experiments could be undertaken with relative safety. Public involvement in the process

"... I do not believe it is in the public interest to insist that a scholarly search for fundamental knowledge be justified in terms of immediate public benefits ..."

would occur by the currently available mechanisms of nonscientist participation on the national Councils concerned with the funding of scientific research. In addition, the local committees assigned to inspect the safety procedures employed by individual scientists could also include publicly-appointed non-scientist members; however, a professionally-trained equivalent of the radiation safety officer might be preferable. Such procedures are desirable, adequate, and appropriate to ensure public safety in this area of research.

Defining Public Interest

Clearly, it is the public's prerogative to specify the extent of its resources that are to be devoted to the support of basic scientific research, and in fact the public exercises this prerogative through legislative bodies. Certainly, it is the public's right to be assured that scientific experiments are carried out safely. It is also the public's right and responsibility to determine directly through various mechanisms how knowledge acquired through basic scientific research is to be applied within the public domain.

While the public also has the right and the means to make primary decisions about the merit of basic scientific research that it supports, I believe that the goals of society as a whole are best served by delegating this responsibility to the present system of scientific peer review. Moreover, I do not be-

"... It would be contrary to the public interest if the initiative of the scientific community in raising issues of experimental safety should lead to a decision by the public to direct the scientific course of such investigations."

lieve it is in the public interest to insist that a scholarly search for fundamental knowledge be justified in terms of immediate public benefits—or to require that basic scientific research become an instrument for the pursuit of short-range political, economic or social goals.

Accelerating Scientific Pace

The pool of bacterial and viral hereditary material on this planet is in a state of constant evolutionary flux, and the activities of modern society have accelerated the pace of natural genetic change. In recent years, naturally occurring antibiotic resistant bacteria have appeared with increasing frequency in response to the widespread clinical use of these drugs. Bacteria and viruses of increasing natural virulence continue to threaten the health of the public. I know of no way to halt these events, but there are means of

Continued on page 16

Fiscal Crisis Worsens at Italian Hospitals

Medical Tribune World Service

ROME—Italy's long-plagued hospital system is suffering additional financial and clinical setbacks as drug companies, hospital suppliers, and bio-medical groups refuse to meet urgent demands for items ranging from heart valves to oxygen for incubators.

Despite allocation of emergency government funds to assist Italy's 1,300 financially strapped public hospitals, doctors and hospital administrators often must dig into their own pockets to satisfy suppliers who demand immediate payment.

Recently at Rome's "Umberto Primo" polyclinic Pediatrics and Obstetrics Division 30 premature infants nearly ran out of oxygen for their incubators. Repeated urgent requests to the supplier were rejected because of past debts running into thousands of dollars. Two thousand liters of oxygen were delivered only when the hospital's secretary signed a personal check for \$1,500.

Purchase Complaints

Dr. Gaetano Azzolina, a cardiologist at Massa Carrara Hospital, complained that he has occasionally had to buy heart valves for operations on a personal basis because the supply houses have refused to furnish them in the face of enormous past debts.

Dr. Azzolina, who has in the past denounced Italy's hospital system, said that in addition to lacking heart valves, many hospitals are short of electrocoagulators and hemodialysis filters, and even gauze, bandages, and x-ray film.

"The sick funds, with their mad organizational structures, are the cause of this rot," Dr. Azzolina said.

He noted that the hospitals are owed about \$6.5 billion by Italy's sick funds, headed by I.N.A.M., which insures about 70 per cent of the population. But because of a lack of payment, the hospitals are often forced to turn to banks for cash at high interest rates.

"Now the banks have no additional funds to give to the hospitals: if the hospitals were normal businesses they would have to declare bankruptcy despite enormous credits," Dr. Azzolina said.

Debts Go Unsettled

A spokesman for A.S.T.R.U., an association of 140 bio-medical and surgery supply companies, said that the hospitals owe about \$400 million for past services. Despite constant pressure on both the hospitals and the government, none of the debts have been settled.

An emergency act by the Italian government in January authorized about \$3 billion in bank credits to pay off the accrued debt. However, slow government machinery and a reluctance on the part of banks to underwrite the credits have further delayed the urgently needed cash flow.

"If it has not failed yet, the Italian hospital is nevertheless completely discredited, both with the banks and the supply houses," Dr. Azzolina noted.

Drug wholesalers have also declared a "state of agitation" towards the hospitals. With debts of millions of dollars

they have threatened to cut off supplies to both hospitals and pharmacies until action is taken.

Vincenzo La Russa, president of the Regina Elena Hospital of Milan, said that much of the situation is caused by poor government control, length of patient hospital stay and lack of hospital beds.

Mr. La Russa said that in 1972 alone, I.N.A.M. spent about \$4.7 billion for 36 million insured persons—more than the United Kingdom spent for all of its insured national program with 50 million people.

"The average Italian hospital stay per person is 16.5 days, reaching a time length unknown to all other Western European countries," he said.

Despite this over-stay in hospitals, in Milan alone there are only 13,500 beds in public hospitals and 3,200 in private hospitals. With a population of over two million, Milan should have 21,000 hospital beds, he noted.

Misuse of Beds Cited

Bad management and poor usage of available space misuses 4,500 existing hospital beds, he added.

Problems plaguing Milanese hospitals, where for example at the 271-bed Sesto San Giovanni Hospital only 23 patients are admitted each day and dozens of other patients are turned away or placed on a waiting list, are found throughout Italy. In one extreme case, a patient earmarked for surgery at

a hospital in Palermo had to bring a bed from home before being admitted.

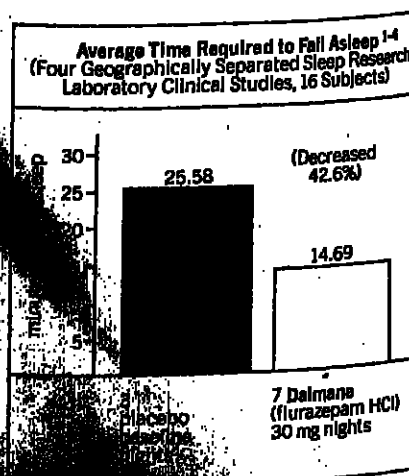
Lack of cash on hand does not only affect the public hospital system's activities with drug companies and medical supply houses, Green grocers, milk companies and bakers have also complained of lack of payment.

While the situation is reaching a critical point, the Italian government headed by Premier Aldo Moro is struggling to put through a sanitation reform program. A first step towards an overhaul of the present health system—which dates to the end of the 19th century—was taken earlier this year with creation of a regional financial control approach for the public hospitals. Under the program, national funds are distributed by region, based on population and need, and are directly overseen by local government.

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Director-General Points WHO Toward a Pragmatic Course

Medical Tribune World Service

GENEVA—World Health Organization strategies are likely to be less traditional and more pragmatic, Dr. Halfdan Mahler, director-general, made clear to the World Health Assembly.

In what looked like a veiled criticism of his predecessor, Dr. Marcellino Candau, he said that W.H.O. planning since the war has been based on "unselective" transfer of technologies from the more technically developed to the poorer countries.

This model of health development has proved difficult to apply and even counterproductive, he declared.

Dr. Mahler said that conventional

medical wisdom has been propagated as the only wisdom throughout the world, and that there has been too much emphasis on scientific accuracy and technical proficiency.

"Is it wise," he asked, "to devote so much effort to what is often only a trivial deepening of technical knowledge rather than to widening the range and increasing the number of beneficiaries through the practical application of what is already known?"

"The very sophistication of today's medical wisdom," he said, "tends to prevent that individual and community participation without which health often becomes a technological mockery."



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... brief summaries of editorials or comments in current medical and scientific journals.

No Teratogenic Effect

"In a follow-up study of 50,282 pregnancies... and the offspring, malformations identified before the fourth birthday, or at death before the fourth birthday, were identified in 3248 children (6.5 per cent). A total of 1870 children exposed in utero to meprobamate or chlorthalidone were compared with 48,412 children who were not. No significant differences were found either overall or in specific outcomes; rates were also similar when exposures occurred during the first trimester or at other times during pregnancy. Deaths (stillbirth to the fourth birthday) occurred in 2227 children (4.4 per cent), and there was no evidence that antenatal exposure to either drug increased the death rate. Finally, as judged by mental and motor scores at the age of eight months, and intelligence quotient scores at four years, there was no evidence that the drugs cause brain damage.

"In this follow-up study there was no evidence that either meprobamate or chlorthalidone, taken at any time during pregnancy, is teratogenic. This observation applied to malformations in general, to malformations that from embryological considerations could only develop in the first trimester, and to defects that could develop either early or late during gestation. Cardiac malformations, in particular, were not associated with early exposure....

"In addition to being unable to confirm a teratogenic effect, we found no evidence that the drugs are related to stillbirth or neonatal, infant or childhood mortality....

"Our findings differ from those reported by Milkovich and van den Berg (*N. Engl. J. M.* 291:1268, 1974)... Perhaps the most important difference between the two studies was that we controlled the analyses for potential confounding by a wide variety of risk-factors for having a malformed child. The comparison groups analyzed by Milkovich and van den Berg consisted of mothers who had documented anxiety. Potential confounding from factors other than anxiety was not controlled. If the relevant factors had been controlled, it is possible that they could have eliminated the associations. An alternative possibility is that the associations reported by Milkovich and van den Berg could have been due to chance. (*Article, Stuart C. Hartz, et al. N. Engl. J. M.* 292:726, April 3, 1975)

Pancreas Center at LSU

Medical Tribune Report

NEW ORLEANS—The first national center for the study of cancer of the pancreas is being established here at the Louisiana State University Medical Center, it was announced by Dr. Allen A. Copping, Medical Center chancellor. It will be funded by the National Cancer Institute, which has made a commitment of \$14,500,000 for the next five years.

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5. Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ

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New TB Guidelines Suggest Less Isolation

By THOMAS BULGER
Special Tribune Correspondent

MONTREAL—New guidelines for the prevention and detection of tuberculosis, representing a significant departure from traditional practices, have been prepared by the American Thoracic Society's scientific assembly on tuberculosis.

The new guidelines are, in general, more liberal than previous ones, proposing less isolation and follow-up of infected individuals who undergo an adequate course of chemotherapy, and generally limiting screening programs to those who are thought to be at special risk of infection.

"Twenty years of experience has demonstrated that, given adequate chemotherapy, tuberculosis is a curable disease," Dr. John Sbarbaro, chairman of the scientific assembly on tuberculosis, told the International Conference on Lung Diseases here. He said that new guidelines are merely recognition of that fact, and are intended to bring about the most effective application of the resources available to fight tuberculosis, consistent with present knowledge, therapeutic capabilities, and prevalence rates.

4 General Areas of Concern

The recommendations encompass four general areas of concern: long-term institutional care, the discharge of patients from medical surveillance, screening programs for health care and educational institutions, and investigation of tuberculosis contacts. While the parent body, the American Thoracic Society, has not yet made the recommendations official, they are expected to do so within the next three months.

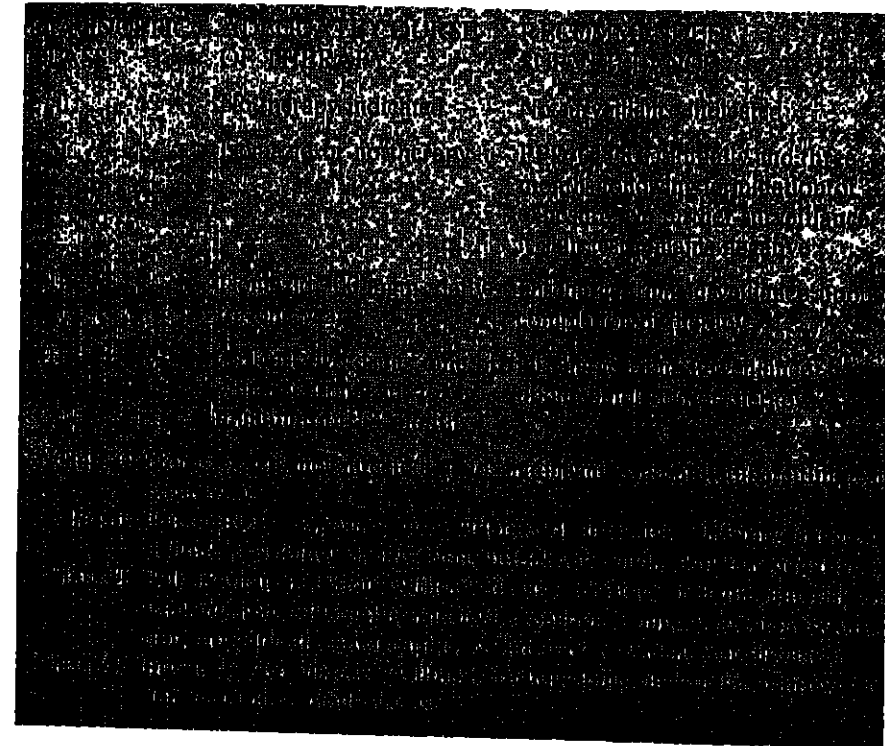
Highlights of the assembly's conclusions and recommendations follow:

• Long-term institutional care.

Since it has been well established that tuberculosis patients receiving adequate chemotherapy are most unlikely to transmit infection, they should be treated in the mainstream of medical care, the assembly said. A small number of patients will require long-term care, usually for reasons unrelated to their tuberculosis, but this can be accomplished safely and efficiently in the long-term care facilities presently in use for patients with other medical or social conditions. Some states have laws restricting tuberculosis patients from these facilities, thereby requiring the maintenance of separate chronic care institutions for this disease, but such restrictions are not justified, according to the assembly.

"In the era of modern chemotherapy, tuberculosis should be treated in whatever setting most appropriately meets the needs of the patient and the community. Some patients can be treated entirely at home. Others may require a short period of hospitalization in a general hospital, followed by ambulatory care. Still others may require longer-term care in an institution, mainly because of other medical and social problems.

"But the fact of tuberculosis should not be the primary determinant of the locale of care, nor should it act as a constraint. . . . A separate, categorical system for tuberculosis care is obsolete."



• Discharge of patients from medical surveillance.

Although frequent relapses are a striking feature of untreated tuberculosis, making periodic evaluations of individuals with the disease important, the assembly said, the accumulated evidence now indicates that adequate therapy not only eradicates the bacilli originally, but makes relapse unlikely. Therefore, the long-term surveillance originally necessary is no longer so, and indeed, dilutes the anti-tuberculosis effort by straining limited resources. The funds are more fruitfully spent ensuring that the original therapy is adequate, the assembly concluded.

Surveillance never worked well anyway. Most relapses were detected when patients entered the standard medical care system with respiratory system complaints, or as incidental findings on physical examinations for other purposes. Prior to discharge from medical surveillance, treated individuals should be educated about the symptoms that might be associated with a relapse, and the importance of their prompt evaluation by a physician.

The table below (above, etc.) summarizes the present definitions of diagnostic categories for tuberculosis, adequate treatment and the new surveillance recommendations for each.

• Institutional screening programs.

The assembly's statement of this subject redefines appropriate screening procedures for in-patients, out-patients, and employees in the general hospital, for extended care facilities, and for schools, kindergartens, nurseries and day care centers. The most significant change concerns the desirability of periodic screening programs for children.

Several pediatric societies have recommended repeating skin tests every two years, but the assembly said that this is a waste of resources; the yield for screening school-age children is generally too low to be practical—less than .05 per cent—as these groups are not at significant risk.

Each child should have one skin test at the earliest point at which he enters the health care system, and then should be retested only when he is thought to be at risk of infection; for example,

when he has symptoms consistent with tuberculosis, is known to have been exposed, or lives in an area in the community of unusually high risk.

The most important and efficient means of protecting children in not repeated testing, but the identification and provision of chemotherapy to infected adults, the assembly said.

• Investigation of tuberculosis contacts.

The likelihood of transmission of the tubercle bacillus depends upon the characteristics of the individual with tuberculosis (source case), of his contacts, and of the environmental air shared between them. Significant questions include:

Source case: Is he receiving chemotherapy? Can tubercle bacilli be isolated from his sputum? Does he cough, and especially, is he unable or unwilling to cover his cough?

Contact: What was the cumulative time of contact? At what physical proximity?

Environmental air: How large was the volume of air in common to the source case and contact? What were the circumstances of ventilation, recirculation, or filtration of the air?

Using the answers to these and similar questions, contacts may be assigned to either low or high risk groups with reasonable accuracy. The assembly then recommends the following guidelines for limiting the extent of contact investigation:

• Evaluate all contacts who present themselves and request study; no one who presents himself in this manner can appropriately be turned away.

• Initiate investigation with higher risk contacts; if there is no evidence among this group of recent transmission of infection, it is appropriate not to extend the investigation.

• If there are data to suggest recent contagion within the higher risk group, the investigation should be extended. To reasonably ensure that the investigation has identified the significant bulk of infections that might be attributed to the source case, progressively lower risk contacts would be evaluated until the level of infection detected approximates the ambient levels of infection within that immediate community.

Clue to Dystrophy?



The muscle structure of a common roundworm may give investigators clues to understanding muscular dystrophies, according to Stanford scientists. Normal muscle, above, has protein filaments in regular parallel patterns. But the muscle of certain mutant nematodes that have been paralyzed by early exposure to high temperatures has thin filaments set at all angles, randomly.

Raw Salad Bacteria Seen Health Peril to Debilitated

Medical Tribune Report

NEW YORK—Opportunistic infections from Enterobacteriaceae on raw salad vegetables may pose a serious threat to debilitated persons, Donald T. Munsey told the 75th annual meeting of the American Society for Microbiology.

Mr. Munsey, research microbiologist at the U.S. Army Natick Development Center, Massachusetts, isolated *Proteus morganii*, *Klebsiella pneumoniae*, *Enterobacter hafniae*, *E. agglomerans*, *E. cloacae*, *Escherichia coli*, and *Citrobacter* from samples of large-scale feeding systems and local retail outlets.

The Natick team also isolated *Pseudomonas aeruginosa*, a special hazard to burn patients. "Healthy individuals should have no problems with any of these organisms," Mr. Munsey said, though they are often eaten with uncooked vegetables.

The study showed that aerobic plate counts and coliforms "had no particular association with the presence of pathogens," and that samples from large-scale feeding systems had greater concentrations of coliforms and fecal coliforms than those from local markets. Mr. Munsey reported no *Salmonella* organisms.

Coauthors were Gerald Silverman, Ph.D., and Barbara Bouchor.

Ovarian Carcinoma Study

Medical Tribune Report

BETHESDA, MD.—Physicians have been asked to refer patients for controlled trials on the use of radiotherapy and chemotherapy following surgery for ovarian carcinoma of all stages.

The study, conducted by the National Cancer Institute's Medicine Branch at the N.I.H. Clinical Center here, is designed to maximize the benefits of available treatment.

Postoperative patients under 65 who have received no therapy other than surgery are eligible for the study.

Malpractice Rates Stiffening In Europe, Except in Britain

Medical Tribune World Service

PARIS—Malpractice insurance rates in Europe are still low, by American standards, but they are beginning to rise. The rate structure in Great Britain represents a notable exception to the trend.

The best bargain is offered by the Medical Defense Union, a prosperous mutual insurance society with 77,000 members in Britain and many other parts of the world. The Union provides sky-the-limit coverage for a flat rate of about \$50.

Rates are sharply higher in France, Germany, and Switzerland. In contrast to the British system, insurers on the continent have a sliding scale according to risk. For a cardiologist in Paris, unlimited cover costs about \$100. But for a physician in a high-risk category, like surgery, anesthesiology, gynecology, or psychiatry, the premium goes up to about \$1,000.

Higher in Germany, Switzerland

In Germany and Switzerland, where most medical insurance is on a straight commercial basis, coverage is less generous and premiums still higher. The amount of insurance is on a graded scale, averaging about \$500,000, and the premium for a physician in an exposed category runs to about \$2,000.

The British society maintains an attitude of studied nonchalance about malpractice suits, which contrasts with the uncoiled anxiety about the future displayed by French and German insurers.

To some extent, the low U.K. tariff appears to reflect the legendary phlegm of the British patient. But a M.D.U. spokesman, Dr. John Wall, also explained that the society adopts a policy that tends to keep it out of expensive lawsuits.

"If a claim is sound, we settle with-

out argument, and the courts know this," Dr. Wall said.

A further constraint on litigation is the fact that contingency fees are considered unethical by the British legal profession.

On the technical side, Dr. Wall pointed out that the British flat-rate system for all members, irrespective of degree of individual risk, also keeps insurance rates down.

"If you separate firemen from other types of driver, you invite a higher insurance premium, and the same goes for a surgeon or gynecologist compared to a general practitioner," he said. "We merge high and low risks into a single rate."

At present, the M.D.U. handles about 350 claims a year and pays out on average about £500,000 annually (about \$1,100,000). Since this represents about one-third of the total income from subscriptions, there are no financial problems.

But in the Montmartre district of Paris, where most French insurance companies have offices—at the bottom of the hill away from the razzle-dazzle—physicians and jurists have recently been holding urgent talks about the level of premiums.

"At present, a French surgeon can get unlimited cover for around 3,000-4,000 francs, or about \$1,000," a spokesman for one of the biggest mutual societies, the picturesquely-named *Le Sou Médical*, explained. "That is less than it costs him to get third-party risk on his Ferrari, but we are losing money on the deal."

Set up in the early 19th century, the society originally charged its members a rate of 1 sou a day, which, at the then rate of 20 sous to the franc, worked out at 18 francs a year.

"Those happy days are gone, and now we are in a very different position,

the L.S.M. official said. "The physician in France is losing his sacrosanct image, and patients are much more aggressive about making legal claims. The French courts also take inflation into account, and so we are seeing a leap in the scale of damages awarded."

Constraints of the type that operate in Britain also hold down the size of awards in France, but the judgments are nevertheless getting steadily bigger.

"We saw a figure of 1,000,000 francs awarded for the first time two years ago," the official commented, "and now

the awards are up to around 3,000,000 francs. Any day we expect to see the first judgment to top 4,000,000, which would be the equivalent of a \$1,000,000 award in the United States."

To make the books balance, rates for the high-risk groups should now be doubled. This was explained by actuaries to the committee of physicians that runs *Le Sou Médical*. But even though such premiums are tax-deductible, the rates are not likely to shoot up so quickly, for psychological reasons.

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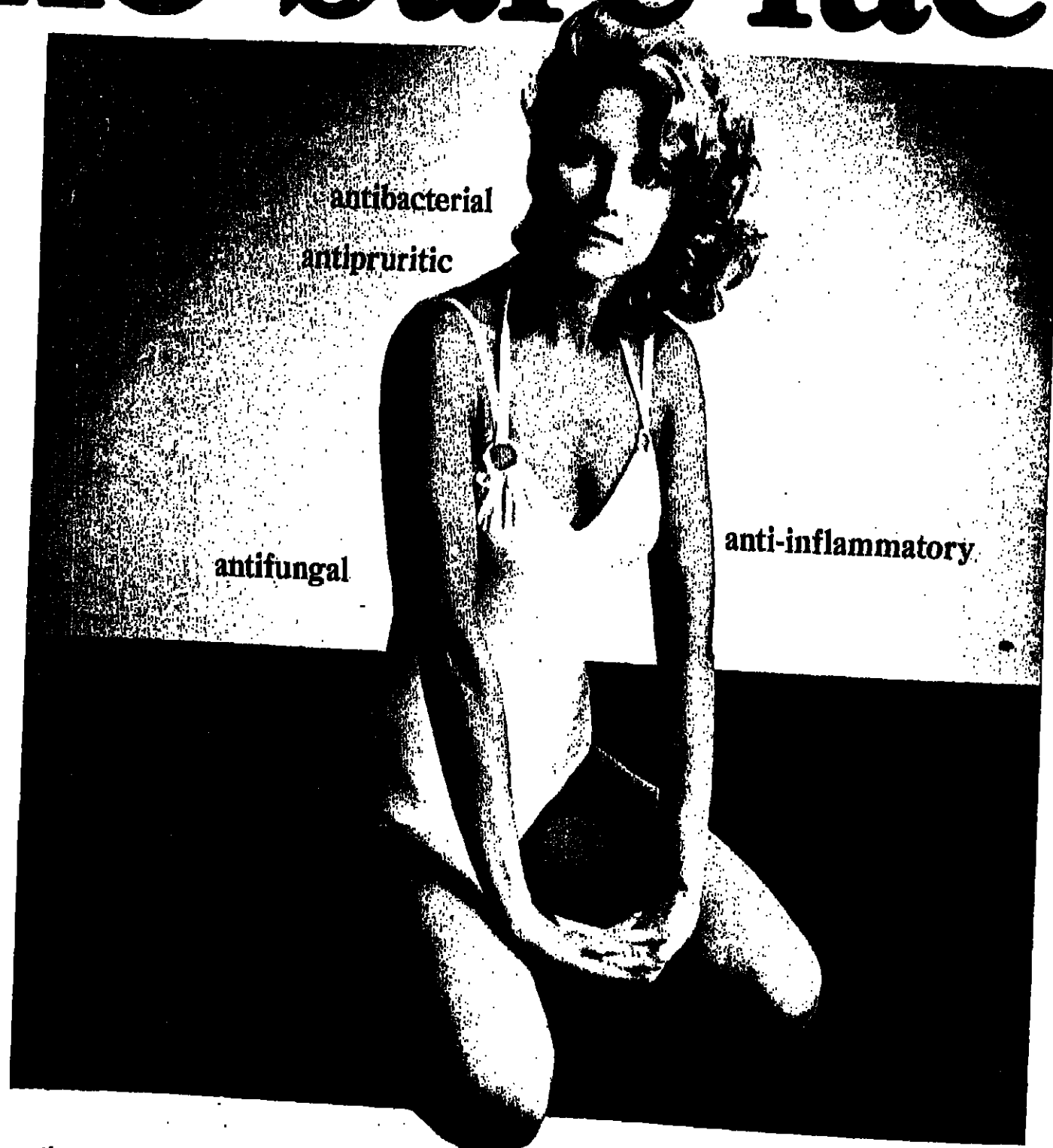
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the bare facts



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INDICATIONS
Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:
"Possibly" effective: Contact or allergic dermatitis; impetigo; eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; localized or disseminated neurodermatitis; lichen simplex chronicus; pruritus (pruritus vulgaris, acral, anal); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, corporis, corporis, pedis); monilia; intertrigo.
Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS
Hypersensitivity to Vioform-Hydrocortisone, or to any of its ingredients or related compounds; viral skin lesions (including herpes simplex, varicella, and varicella).
WARNINGS
This product is not for ophthalmic use.
In the presence of systemic infections, appropriate systemic antibiotics should be used.
Usage in Pregnancy
Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

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May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May cause irritation to sensitized skin in rare cases.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.
May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of non-susceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS
Few reports include: hypersensitivity, local burning, irritation, bruising, discoloration if unwashed reaction occurs. Rarely, topical corticosteroids may cause atrophy at site of application when used for long periods in intertriginous areas.

DOSEAGE
Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED
Cream, 3% Iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing

stearic alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin. In water-washable base: tubes of 5 and 20 gm. Ointment, 3% Iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base: tubes of 5 and 20 gm. Lotion, 3% Iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polyacrylate 60, triethylamine, methyl-2-vinylpyrrolidone, and perfume. Flare in water-washable base: tubes of 5 and 20 gm. Mild Green, 3% Iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearic alcohol, cetyl alcohol, petrolatum, sodium lauryl sulfate, and glycerin.

In water: tubes of 1/2 and 1 ounce. Mild Ointment, 3% Iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base: tubes of 1/2 and 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

7/20/77

Vioform-Hydrocortisone

(iodochlorhydroxyquin and hydrocortisone)

Another fact...
the most widely
prescribed form...
20-Gm Cream

C I B A

Wednesday, July 23, 1975

MEDICAL TRIBUNE

11

The Only Independent Weekly Medical Newspaper in the U.S.

Medical Tribune

and Medical News
Published by Medical Tribune, Inc.

The Dangers of the Dalkon Shield... and the Responsible Actions of FDA

SEVENTEEN DEATHS and a significant morbidity with the Dalkon Shield is a serious matter. There is no need to sensationalize it further with an intimation that the F.D.A. was trying to suppress a Dalkon Shield report.

The mandate of the F.D.A. is defined by law; the scope of its responsibilities is great; the complexity of some of its decisions most difficult. Even though MEDICAL TRIBUNE has differed, disagreed and disputed many of their decisions, the top leadership of the F.D.A. has been, through several administrations, and is now in the hands of men whose personal integrity is beyond challenge. The F.D.A., charged with deciding whether or not a drug or device is safe and effective, must take into consideration all the potentials both for help and harm. It must discharge its functions in a responsible manner, sensitive to feelings of patients, alert to the dangers of panic, and cognizant of the need for informing physicians so that they can advise their patients on

the basis of facts and not hysterical headlines.

In the past, MEDICAL TRIBUNE has felt that too little attention was paid to these all-important considerations with consequent and needless disruption of prophylactic therapeutic regimens and physician-patient relationships. On this occasion the F.D.A. recommended against new insertions of the Dalkon Shield and, in consideration of patients' total well being, arranged to inform physicians fully on the dangers of the Dalkon Shield. Furthermore, it presented its Dalkon Shield report in an open meeting and in a responsible manner; it did not suppress it. The F.D.A. thus acted to protect patients fully—without the creation of panic. It would seem to us that when the F.D.A. takes judicious, considered and deliberate—not panic-inducing—regulatory action, it should merit the praise of the press and not be subjected to misleading, if not malicious, journalistic sensationalism. A.M.S.

Genetic Engineering

ONE OF THE remarkable examples of prospective concern by scientists about possible hazards implicit in their most advanced accomplishments, rather than retrospective dismay and disillusionment, has been the history of the developments culminating in the Asilomar International Conference on Recombinant DNA Molecules. Once it was discovered that DNA could be cleaved at specific sites with the use of certain enzymes and it became clear that it would be possible to "unite" DNA from animal viruses with bacterial DNA, or DNAs of different viral origins might be so joined, certain dangers were envisioned. These were, in short, that certain of the "hybrid" molecules may prove hazardous to laboratory workers and the public.

Following a recommendation by molecular biologists late in 1973 that a "study program be instituted to consider the problem and to recommend specific actions or guidelines," steps were taken that wound up in the Asilomar conference. Dr. Stanley N. Cohen is one of the investigators whose accomplishments led to "the construction in a test tube of biologically functional DNA molecules that combined genetic information from two different sources." As an active participant in the Asilomar conference, Dr. Cohen's testimony on genetic engineering before the Senate Subcommittee on Health, condensed in the *Current*

Opinion of this and the preceding issue of MEDICAL TRIBUNE, is of enormous interest and pertinence.

He observed that while the public "has the right and the means to make primary decisions about the merit of basic scientific research that it supports, I believe that the goals of society as a whole are best served by delegating this responsibility to the present system of scientific peer review. Moreover, I do not believe it is in the public interest to insist that a scholarly search for fundamental knowledge be justified in terms of immediate public benefits—or to require that basic scientific research become an instrument for the pursuit of short-range political, economic or social goals."

Of equal importance is Dr. Cohen's remark that "while it is essential for the public to be assured that experiments seeking knowledge in this area and in other areas of basic science are carried out safely, I believe that it would be contrary to the public interest if the initiative of the scientific community in raising issues of experimental safety should lead to a decision by the public to direct the scientific course of such investigations."

It is the scientists who have pointed out the hazards; who are, worldwide, considering and introducing the methods to contain them; and who are best equipped to direct the scientific course of their investigations.

The Glucagon Relationship

CLINICAL QUOTE: "One cannot help but be impressed with the potential therapeutic efficiency that a safe and practical glucagon-suppressing drug

might offer in the control of diabetic hyperglycemia." (Dr. R. H. Unger, American Diabetes Association meeting; see page 1.)



"Of course, this faith healer isn't for everyone. He specializes in diseases of the cardiovascular system."

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LETTERS TO TRIBUNE

Funds and Beds

Your article on the state of New York City municipal hospitals described the chaos resulting from inadequate funding. A more accurate description would have included a statement of the 50. per cent bed vacancy that prevails in many city hospitals.

SAUL B. GILSON, M.D.
New York

The Care of Veterans

I am happy that Mr. S. M. Appleman, Director of Media Liaison for the Central V.A., took the time (MEDICAL TRIBUNE, May 21) to reply to my letter of March 5. However, I wish he had read my letter more carefully. I spoke of the V.A.'s failure to provide for treatment of delayed post-combat stress reactions ("syndromes"), meaning precisely those beginning more than two years after discharge. Moreover, Mr. Appleman states that "any psychoses [sic] manifested within two years of discharge is presumed to be service-connected." My concern is with the non-psychotic men (always the vast majority) who first develop symptoms more than two years after discharge.

As for there being "no time limit for considering valid evidence of service connection," I know of veterans with impressive documentation who are spending all their free time trying to establish service-connection without success. That is a difficult, expensive route. Moreover, I also know of V.A. professionals in several centers who have learned to their occupational detriment—that it does not pay to "make waves," i.e. to become too strongly identified as advocates of broader treatment criteria for Vietnam veterans with emotional problems.

In some centers the problem is being solved—not on grounds of service-connection—but under a rule allowing outpatient therapy for any veteran if it can be shown that this will prevent hospitalization. Here again, some centers apply

stricter standards to validate that rule than do others.

I think this dialogue is of the utmost importance, not only for the millions of Vietnam-era veterans, but for the future of bureaucratically-administered psychiatry in this country.

Dr. Samuel Johnson (not an M.D.) once said "the road to hell is paved with good intentions."

CHAIM F. SHATAN, M.D., C.M.
Postdoctoral Psychoanalytic
Training Program
New York University
New York

Remember Weismuller?

In response to the piece "Athletes Advised to Develop Agility in Dodging Doctors" (MT June 11), I remember Johnny Weismuller—the great swimmer—having to lay off swimming back in the twenties, I believe, because of what was then termed an "athletic heart."

I wonder if doctors then were treating the ECG rather than the patient?

GEORGE GRAINGER, D.O.
Tyler, Texas

Insurance Suggestion

Re malpractice insurance: Why not shift to the type of *ad hoc* insurance sold at airports and bus stations?

Let the patient figure what he's worth or can afford if he's unhappy with the results of his Blue Cross-paid care; let the insurance actuaries figure out chances of defined poor results per modality or procedure, by hospital and physician, and then let each patient pay his premium—and collect if warranted. Gets rid of lawyers, puts the patient on the spot, and lets him fight the insurance companies, not doctors.

GEORGE BROWNING, M.D.
Penfield, N.Y.

A Psychiatrist's Wife Catches the Spirit of the AMA Convention



The exhibition hall.

IDA LIBBY DENGROVE, the wife of a New York psychiatrist, Dr. Edward Dengrove, is the talented artist through whose eyes millions of television viewers across the nation followed the proceedings during the Mitchell-Stans trial in New York. Her sketches appeared on NBC-TV as her pastel sketches illustrated what the Today show and evening news programs. Mrs. Dengrove called drawing for the entire trial "utterly fantastic" and the most exciting thing she has ever done. Recently, Mrs. Dengrove, her husband, and one of their sons finished medical school attended the American Medical Association annual convention in Atlantic City. Long active in the medical community, Mrs. Dengrove has served as arts and hobbies chairman for New Jersey and has encouraged other doctors' wives to develop their artistic talents. She has also done sketches of the convention and its participants.



Dr. Edward Dengrove and son, Dr. Robert Dengrove.



Dr. and Mrs. Donald Haselhuhn of Camp Hill, Pa.



Dr. and Mrs. Romed Ferrer and family from Glen Burnie, Md.



On the panel, Dr. Wittig (left) of Gainesville, Fla., and Sanford Chodosh, of Boston University School of Medicine, Dr. Stephen Lockey (lower left) of Lancaster, Pa.



Physician registration.

LIBRIUM® AT WORK: (chlordiazepoxide HCl)

B.W.: A CASE IN POINT*

PATIENT: 51-year-old male, Caucasian; married; one son, 12 years old; occupation: sales manager.

FAMILY HISTORY: Father hypertensive; cause of death, possible MI; grandmother diabetic.

PAST HISTORY: Prior to current illness exercised regularly, tennis 2-3x/week; smokes heavily (over 2 packs/day). Remainder of medical history noncontributory. States he enjoyed good health in past—no known history of hypertensive, cardiovascular or pulmonary disease.

RECENT HISTORY: Hospitalized eight weeks previously with diagnosed acute MI.

CLINICAL COURSE: Uneventful recovery; discharged 26 days following hospital admission. Four weeks of gradually increasing activity at home. Complete evaluation scheduled prior to returning to work.

CURRENT FINDINGS: About 15 lbs overweight; admits to high fat and carbohydrate intake. Upon examination, the patient was apprehensive; markedly reactive to all somatic sensations. Concern expressed about transient headaches being "stroke" symptoms. Physical examination normal. EKG showed normal sinus rhythm with typical evolution of abnormalities consistent with healing of the infarct.

MEDICAL MANAGEMENT: In addition to medical regimen, Librium 10 mg t.i.d.; continued for 2 months to relieve anxiety.

COMMENTS: Despite excellent response to medical regimen and objective evidence of full recovery, return to full normal activity inhibited by patient's excessive anxiety. Antianxiety medication reduced this to manageable levels.

*Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley, New Jersey. Although this is an actual case history, not all cases of organic cardiovascular disease can be expected to have the same response to therapy.

IN THE ANXIOUS PATIENT
WITH ORGANIC CARDIOVASCULAR
DISEASE

WHEN CLINICAL ANXIETY EXACERBATES AN ORGANIC DISORDER

During cardiac convalescence, the patient's anxieties can often be allayed through your reassurance and counseling and his family's encouragement and support. In some patients, however, excessive anxiety can interfere with progress. When this occurs, Librium (chlordiazepoxide HCl) may be a beneficial adjunct to total management.

Librium offers a high degree of antianxiety effectiveness and is used as an adjunct to primary cardiovascular medications. It also provides a wide margin of safety. In proper dosage, Librium usually helps calm the overanxious patient without unduly interfering with mental acuity or general performance. Initial therapy should be limited to the smallest effective dosage, particularly in the elderly and debilitated patient, to preclude development of ataxia or over-sedation. And Librium therapy should be discontinued when anxiety has been reduced to tolerable levels.

Librium is used concomitantly with certain medications of other classes of drugs, such as cardiac glycosides, diuretics, antihypertensive agents, vasodilators and anticoagulants. While rare reports of variable effects on blood coagulation in patients receiving oral anticoagulants and Librium have been noted, clinical studies have not established a cause and effect relationship.

WHEN CLINICAL ANXIETY INTERFERES WITH THERAPEUTIC PROGRESS

LIBRIUM®
chlordiazepoxide HCl/Roche
5 mg, 10 mg, 25 mg capsules
FOR ALL THE RIGHT REASONS

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation or in women of child-bearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients, and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Moderate Position on PSROs Prevails at AMA Convention

Continued from page 1

activities, on grounds that it was unconstitutional. At the A.M.A. meeting several delegates, among them Dr. Michael Smith, President, Louisiana State Medical Society, hailed the ruling as a turning point in the fight against governmental interference in medical practice, and an indication that the time was ripe for P.S.R.O. repeal.

However, Dr. Russell Roth, past president of the A.M.A., said that the injunction might be reversed on appeal. And he warned that if P.S.R.O. were killed, another federal law would "inevitably" take its place, which "could be even worse than the one we have to deal with now."

Nevertheless, a good deal of discussion could be heard in the corridors of the convention, if not on the House of Delegates floor, expressing hopeful speculation that the Hoffman ruling might lead to a Supreme Court decision on a pending suit of the American College of Surgeons against H.E.W., that would find P.S.R.O. unconstitutional in its entirety.

Some delegates also mentioned the well-known funding woes of P.S.R.O., and wondered whether the plan might not soon die a quiet death from fiscal malnutrition.

Official Policy About the Same

In the meantime, official A.M.A. policy and recommendations, as approved by voting on resolutions, stayed pretty much the same as before.

A number of resolutions introduced by Dr. Frank A. Rogers of California and supported by delegates from Louisiana and Oklahoma, that would have had the A.M.A. mount a campaign for the repeal of P.S.R.O. and advise doctors not to comply with existing programs, were turned back by comfortable margins.

In arguing for his resolutions, Dr. Rogers said that "delaying tactics will not pay off." Local peer review, he declared, "is just a temporary expedient. We should all know by now that once P.S.R.O.s are in place, peer utilization boards will simply be pre-empted, and local regulation will be supplanted by federal regulation."

But most delegates seemed to agree with the report of the A.M.A. special reference committee, chaired by Dr. George H. Mills of Hawaii and assigned to hear testimony on the P.S.R.O. matter, that "repeal does not present a realistic alternative at this point." Instead the committee recommended a "policy statement" reaffirming last year's stand—which, it was emphasized, "does not preclude individual state associations from electing non-participation." This statement was passed.

Its pragmatic nature was noted by Dr. Max H. Parrott, newly-installed A.M.A. president, in his inaugural address.

"The A.M.A. has become more aggressive of late, as instanced by our first lawsuit against the federal government, the suit over the utilization-review regulations," he said. "We need to be even more aggressive. But our effectiveness depends not only on the will to act, but on the capacity to act."

Complete non-cooperation with P.S.R.O. at this time would be politically unwise, possibly illegal, and certainly contrary to the A.M.A.'s "humanistic belief in the individual patient and his quality of care," Dr. Parrott stated.

While delegates voted to counsel physicians to continue abiding by P.S.R.O. laws, to monitor their effects and lobby for amendments that would guarantee local autonomy, they made a

distinction between voluntary peer review, which is nearly universal, and mandatory procedures, which are in actual operation in less than half of the areas of the nation designated by H.E.W.

The House overwhelmingly supported a resolution that called for physicians to serve on voluntary boards of their own creation without pay, but to require "compensation when providing their time and expertise" to review boards involving the government or other third parties.



Opening session of the A.M.A. House of Delegates.

Up to 3,100,000 Estimated to Suffer Ankylosing Spondylitis

Continued from page 1

These admittedly "rather extraordinary statements" were made to the American Rheumatism Association Section of The Arthritis Foundation by Drs. Andrei Calin and James F. Fries. They said important benefits would follow increased awareness and screening because AS symptoms respond readily to relatively safe, non-steroidal anti-inflammatory agents.

Their finds grew out of an investigation made in an effort to establish the actual prevalence of AS among the 7 per cent of the Caucasian population of the United States having the histocompatibility antigen HLA-W27.

Twenty-four hundred healthy blood donors were examined in the Stanford study. Among these Drs. Calin and Fries found 120 with the W27 marker. They were matched by race, sex and age with 190 controls who are W27 negative. Seventy-eight positive subjects cooperated, as did 126 controls.

History of Back Pain

Twenty-two (28.2 per cent) of the positives reported a history of back pain, compared with 11 (8.7 per cent) of the controls. Of the 22 with W27, 59 per cent had sleep disturbances, 82 per cent morning stiffness and 73 per cent relief with exercise—symptoms of AS.

None of the controls with back pain had any of these symptoms, and their back pain was diagnosed as mechanical, rather than inflammatory as in the W27 group.

Rather than subject the asymptomatic controls to x-ray, the Stanford physicians randomly selected 36 control films from patients who had under-

gone radiological investigation such as barium studies and pyelograms. These films were reviewed blindly along with the films of 19 W27 subjects with back pain. Fourteen of the W27 group were found to have definite AS by the New York criteria for radiological changes. Not one of the controls met the criteria.

Of the 78 cooperating W27 subjects, 27 per cent of the females and 30 per cent of the males had back pain. In the radiological test, 8 females (16.7 per cent) and 6 males (20 per cent) had AS.

AS in 20% of W27-Positive Men

Dr. Calin said the expected prevalence of AS in the W27 positive community is 2 per cent for males and 0.2 per cent for females. "Instead," he continued, "20 per cent of our male subjects and 17 per cent of the women studied had definite and symptomatic AS. It is possible that these figures represent an underestimate. There were further subjects, symptomatic for back pain, with a history suggesting inflammatory disease, but unavailable for clinical or radiological investigation. Furthermore, the exclusion of individuals with known ankylosing spondylitis continues to underplay these results."

He cited other studies with conclusions which agree with the Stanford suggestion that there is a prevalence of AS in the W27 community of 20 per cent—a figure 10 times the expected frequency in males and 80 times in females.

"If 20 per cent of W27 positive subjects have undiagnosed AS and W27 is present in 7 per cent of the population, then undiagnosed AS is present in 1.4

per cent of the population," Drs. Calin and Fries suggested.

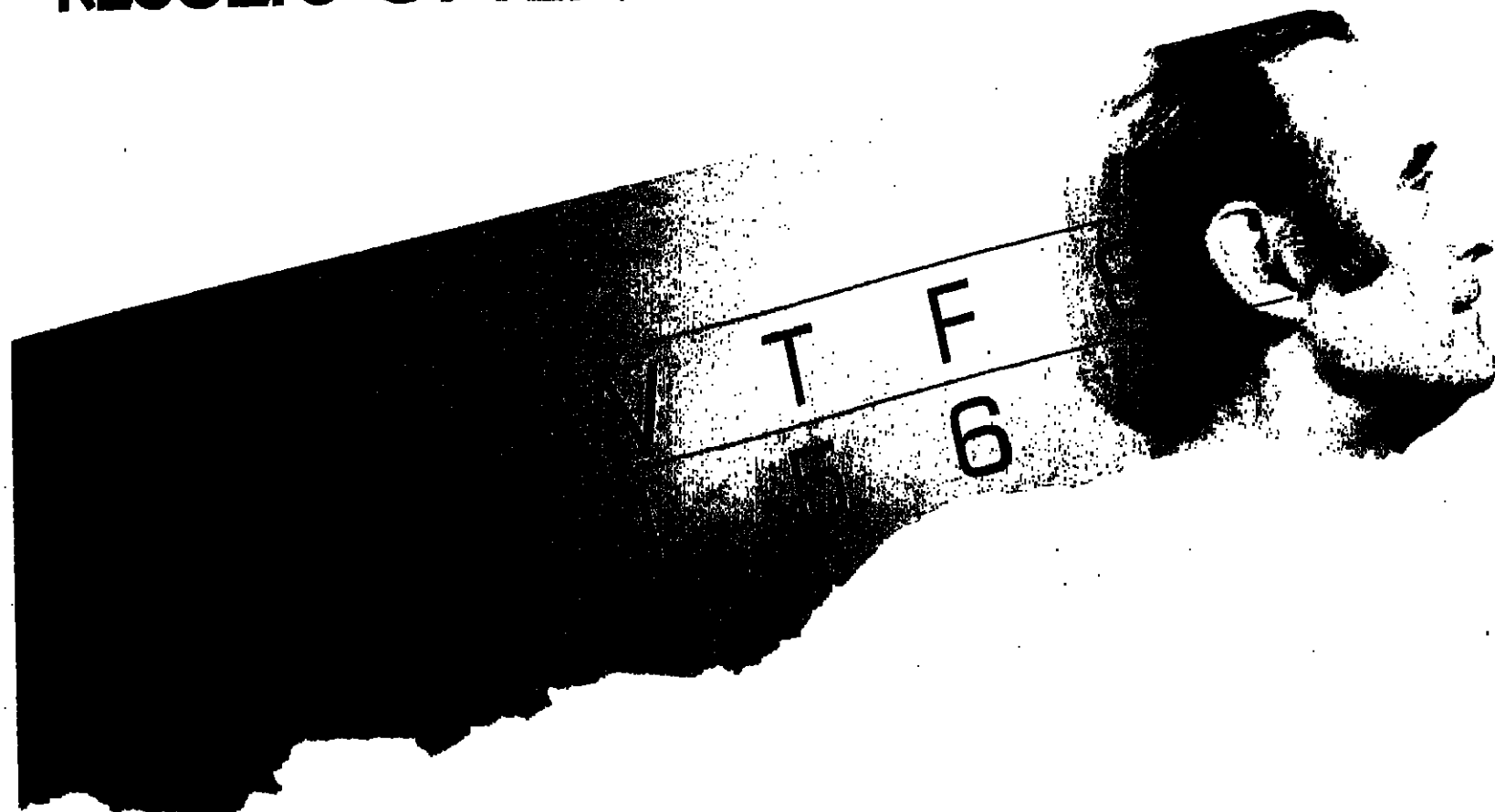
Dr. Fries noted that many women may think their AS symptoms are menstrual cramps. He noted that the disease tends to be milder in women, whose outside joints are more involved. A reluctance to subject women of child-bearing age to radiation may result in the diagnosis being missed frequently, he added.



MELLARIL® (THIORIDAZINE)

TABLETS: 10 mg, 15 mg, and 25 mg thioridazine HCl, U.S.P.

IN CLINICALLY SIGNIFICANT DEPRESSIVE NEUROSIS—RESULTS OFTEN SEEN IN A WEEK



Mellaril can often help you give patients with depressive neurosis relief within a week. In 14 double-blind studies of four weeks duration, 339 patients with depressive neurosis received Mellaril. In these studies, 55% of the overall improvement was observed by the end of the first week, and a total of 293 patients (86%) improved during the four weeks.*

With Mellaril, patients often have an end to such symptoms as insomnia, G.I. symptoms, irritability, dejection, and hopelessness before they have a chance to become entrenched.

*Data on file at Sandoz Pharmaceuticals.

Mellaril (thioridazine) short-term therapy of moderate to marked depression with variable degrees of anxiety in patients with depressive neurosis

Before prescribing or administering, see Sandoz literature for full product information. The following is a brief summary:

Contraindications: Severe central nervous system depression, comatose states from any cause, hypotensive or hypotensive heart disease of extreme degree.

Warnings: Administer cautiously to patients who have previously exhibited a hypersensitivity reaction (e.g., blood dyscrasias, jaundice) to phenothiazines. Phenothiazines are capable of potentiating central nervous system depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorus insecticides; carefully consider benefit versus risk in less severe disorders. During pregnancy, administer only when the potential benefits exceed the possible risks to mother and fetus.

Precautions: There have been infrequent reports of leukopenia and/or agranulocytosis and convulsive seizures. In epileptic patients, anticonvulsant medication should also be maintained. Pigmentary retinopathy, observed primarily in patients receiving larger than recommended doses, is characterized by diminution of visual acuity, brownish coloring of vision, and impairment of night vision; the possibility of its occurrence may be reduced by remaining within recommended dosage limits. Administer cautiously to patients participating in activities requiring complete mental alertness (e.g., driving, and increase dosage gradually. Orthostatic hypotension is more common in females than in males. Do not use epinephrine in treating drug-induced hypotension since phenothiazines may induce a reversed epinephrine effect on occasion. Daily doses in excess of 300 mg should be used only in severe neuropsychiatric conditions.

Adverse Reactions: Central Nervous System—Drowsiness, especially with large doses, early in treatment. Infrequently, pseudoparkinsonism and other extrapyramidal symptoms; rarely, nocturnal

confusion, hyperactivity, lethargy, psychotic reactions, restlessness, and headache. **Autonomic Nervous System—**Dryness of mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal stuffiness, and pallor. **Endocrine System—**Galactorrhea, breast engorgement, amenorrhea, inhibition of ejaculation, and peripheral edema. **Skin—**Dermatitis and skin eruptions of the urticarial type, photosensitivity. **Cardiovascular System—**ECG changes (see Cardiovascular Effects below). **Other—**Rare cases described as parotid swelling. **The following reactions have occurred with phenothiazines and should be considered: Autonomic Reactions—**Miosis, constipation, anorexia, paralytic ileus. **Cardiac Reactions—**Agranulocytosis, leukopenia, contact dermatitis. **Blood Dyscrasias—**Agranulocytosis, leukopenia, eosinophilia, thrombocytopenia, anemia, aplastic anemia, pancytopenia. **Allergic Reactions—**Fever, lymphatic edema, angioneurotic edema, asthma. **Hepatotoxicity—**Jaundice, biliary stasis. **Cardiovascular Effects—**Changes in terminal portion of electrocardiogram, including prolongation of QT interval, lowering of T-wave, and appearance of a wave tentatively identified as a T or U wave have been observed with phenothiazines, including Mellaril (thioridazine); these appear to be reversible and due to altered repolarization, not myocardial damage. While there is no evidence of a causal relationship between these changes and significant disturbance of cardiac rhythm, several cases of unexpected deaths apparently due to cardiac arrest have occurred in patients showing characteristic electrocardiographic changes while taking the drug. While proposed, periodic electrocardiograms are not regarded as predictive. Hypotension, rarely resulting in cardiac arrest. **Extrapyramidal Symptoms—**Tachycardia, agitation, motor restlessness, dystonic reactions, tics, tardive dyskinesia, oculogyric crises, tremor, muscular rigidity and ataxia. **Parosmia**

Tardive Dyskinesia—Persistent and sometimes irreversible tardive dyskinesia, characterized by rhythmic involuntary movements of the tongue, face, mouth, or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements) and sometimes of extralimbic muscles may occur on long-term therapy or after discontinuation of therapy, the risk being greater in elderly patients on high-dose therapy, especially females; if symptoms appear, discontinue all antipsychotic agents. Syndrome may be masked if treatment is instituted, dosage is increased, or antipsychotic agent is switched. Fine vermicular movements of tongue may be an early sign, and syndrome may not develop if medication is stopped at that time. **Endocrine Disturbances—**Menstrual irregularities, altered libido, gynecomastia, lactation, weight gain, edema, false positive pregnancy tests. **Urinary Disturbances—**Retention, incontinence. **Others** include: behavioral effects suggestive of a paradoxical reaction, including excitement, bizarre dreams, aggravation of psychosis, and toxic confusional states; following long-term treatment, a peculiar skin-eye syndrome marked by discoloration of exposed sclera and conjunctiva and/or accompanied by opacities of anterior lens and cornea; systemic lupus erythematosus-like syndrome. **Dosage:** Dosage must be individualized according to the degree of mental and emotional disturbance, and the smallest effective dosage should be determined for each patient. In adults with depressive neurosis the usual starting dosage is 25 mg b.i.d. and the dosage ranges from 10 mg b.i.d. to q.i.d. for more severely ill patients; the total daily dose ranges from 20 mg to a maximum of 200 mg.

SANDOZ PHARMACEUTICALS, EAST HANOVER, NEW JERSEY 07630



One Man...and Medicine

ARTHUR M. SACKLER, M.D.
International Publisher, Medical Tribune



The Danger of Double Standard

ANY USE OF A double standard is unfair; in science it is anti-science, and in public health it can be deadly dangerous. The difference with which contraceptive, as compared to therapeutic, technology is treated in the press and the political arena results in regulatory inconsistencies affecting controls on substances as diverse as the commonplace cyclamates and the most critical cardiovascular medicinals.

Even though not a single human death was traced to the cyclamates and though a huge mortality and morbidity are attributable to obesity (in whose management cyclamates are indicated), the single, uncorroborated finding of bladder cancer in a study of rats led to the removal of cyclamates from drug store shelves. MEDICAL TRIBUNE protested that action and pointed out that saccharin, implicated with the cyclamates, was not subjected to regulatory banishment.

Case of Beta-Blockers

Clinical pharmacologic research on the beta blockers, potentially very important life-saving agents in critical cardiovascular states, has been deferred for almost two years on the basis of animal malignancies reported with one agent. It would not be surprising if serious side effects can be provoked in animals by massive and even less than massive dosages of cardiovascular drugs. After all, they are not inert substances. It would not be surprising if side effects occur in man—after all, they occur with morphine, digitalis, and oxygen, three of the most common agents used to combat the greatest killer of all, cardiovascular disease. But in respect to one of these we confront the added inconsistency of general drug store availability of one beta blocker and the interdiction of basic clinical pharmacologic studies even under the most controlled conditions by highly qualified investigators on others.

We concur on the need for caution in respect to all substances given to man. But we believe that we should respect considered judgments, recognizing that calculated risks must always be consciously and conscientiously weighed against clinical benefits—for that is the essence of medical decisions. Such are the daily responsibilities of every practicing physician in this country, as well as of the F.D.A.

Popular "Crisis"

On the other hand, we do not believe that popular concern over the highly propagandized "population crisis" should invalidate scientific logic or call for lower standards in judgments when these affect contraceptive technology. There are alternatives to the Dalkon Shield; there are choices other than sterilization; The Pill is not the sole or indispensable measure. Other means are effective and have had a long history of use. The argument as to the incidence of side effects in pregnancy or

maternal deaths are pertinent but not determinative. The social desirability of population control should not dilute scientific standards or medical safeguards in relation to contraceptive measures; yet they do because of press approbation and popular pressures.

There are more than half a million U.S. deaths a year (683,100) due to coronary disease alone, compared to 15,200 deaths in childbirth, yet it has been almost impossible to clear cardiovascular agents in the same period that variation after variation of The Pill have obtained F.D.A. blessing and gone to market. Government officials and political figures will give you a plethora of excuses for the continuing promotion as well as constant propagation of new formulations of the two most toxic substances responsible for the largest number of preventable deaths and disabilities—alcohol and tobacco. Yet they pursue to the point of persecution the phantasy of therapeutic agents sans side effects and sans risk.

Some Real Hazardous Drugs

If the press is really concerned about our national health and about the death and suffering of our patients, then it can take a part in saving lives without new legislation—by simply refusing to accept advertising for death-dealing alcohol and tobacco. There is no question as to their cardiotoxicity, cerebrototoxicity, hepatotoxicity and carcinogenicity; there is no question of their habit-forming, dependency provoking or, if you wish, "addicting" potentials in man, not just experimental animals. Failure to recognize these facts and to act upon them suggests a pious hypocrisy manifested by expressions of concern for the public health while pocketing profits through participation in the sale of death-dealing agents. We have enough problems in America without the constant utilization of different standards. Double standards are pernicious socially, illogical scientifically, and unacceptable medically, particularly when lives are at stake.

EPICRAMS—Clinical and Otherwise

Although human life is priceless, we always act as if something had a even greater price than life... but what is that something?

Antônio de Vól de Nult
(1900-1944)
in Saint Exupéry

Labeled Antimyosin Antibody New Avenue to Infarct Study

Medical Tribune Reports

ATLANTIC CITY, N.J.—A new approach to localization and sizing of myocardial infarcts that would be based on the ability of labeled antibody specific for cardiac myosin to concentrate in infarcted tissues was reported here by investigators from the Cardiac Unit of Massachusetts General Hospital, Boston.

Such concentration of labeled anti-myosin antibody has now been demonstrated in dogs with experimentally produced infarction, Ben An Khaw, Ph.D., Research Fellow, told the American Society for Clinical Investigation.

Dr. Khaw said the concentration occurs "presumably" because the cellular permeability induced by ischemia enables antibody to enter the damaged area.

In the animal studies, canine cardiac myosin was injected into rabbits. The resulting specific antibody was purified by affinity chromatography and labeled with ¹²⁵I. Dogs with acute infarction received an intravenous injection of rabbit immunoglobulin 3 1/2 hours after the last ligation, followed in 30 minutes by an I.V. injection of the labeled anti-myosin antibody.

Examination of myocardium samples obtained from animals sacrificed 18 hours later showed a significantly higher concentration of the anti-myosin antibody in the center and periphery of the infarct zone than in normal myocardium, Dr. Khaw said.

Even border zone concentration of this antibody was significantly higher than that in normal myocardium, and localization was higher in endocardial layers of infarcted myocardium than in epicardial layers.

Fragment of Antibody Used

Another experiment employed a fragment of the whole antibody from which the "sticky" third of the molecule had been removed by treatment with pepsin. Specificity of localization with the ¹²⁵I-labeled fragment was enhanced two and one-half fold compared to that of whole antibody.

To determine if localization was specific, the investigators conducted a test in which animals were injected simultaneously with anti-myosin antibody fragments labeled with ¹²⁵I and with nonspecific immunoglobulin fragments labeled with ¹³¹I. Localization proved both specific and selective.

Dr. Khaw also reported that a study of anti-myosin antibody and regional blood flow, using ¹²⁵I-labeled specific antibody fragments and ⁸⁶Sr-labeled microspheres, demonstrated conclusively that relative antibody concentration increases as flow decreases.

Dr. Edgar Haber, a member of the investigative team and Professor of Medicine at Harvard Medical School, emphasized during a news conference that research on this possible approach to infarct localization and sizing is still at its earliest stage of development and "is by no means ready" for application in clinical practice.

He does, however, view the prospects as encouraging since the animal

experiments show "an unusual degree" of anti-myosin antibody concentration in the infarct center, and such concentration is specific.

What the team now hopes to do, he said, is to label the myosin-specific antibody with an isotope that allows for scanning. Noting that the isotope ¹²⁵I has radiation properties suitable for localization, he pointed out that devices such as a gamma camera now make it possible to take a picture of a patient and determine where radioactivity is localized.

One major hurdle to overcome is that of foreign protein, Dr. Haber continued. But he suggests that this does not seem an "insuperable" problem since only a few micrograms of myosin-specific antibody would probably prove necessary.

Long Experience Noted

"We already have experience with introducing antibody into man in other circumstances," he said. "For example, in the treatment of organ rejection, antilymphocyte globulin in gram amounts have been used for years without serious ill effects."

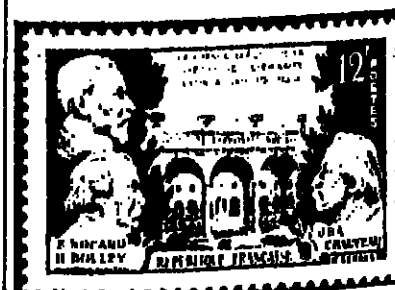
The next stage in development—which Dr. Haber expects to get underway within the next two months—will be to see if the right isotope can be put on the specific antibody so that a picture can be taken of canine infarction.

"If we can do that," he said, "the next step is to work out methods for applying this procedure to man."

Other authors of the report were Drs. G. A. Beller and T. W. Smith.

Medicine on Stamps

Nocard, Bouley, Chaveau



Stamp issued by France to honor three famous scientists in the field of veterinary medicine. Edmond Nocard was associated with Pasteur, discovered the virus of parrot fever, and with Roux studied Actinomyces. Henri Bouley was inspector general of all French animal husbandry schools. Served as president of the French Academy of Medicine and was considered one of the best authorities on the diagnosis and treatment of animal diseases. Jean Chaveau is best known for his investigation of heat and energy relations in muscular work and his studies of immunity mechanisms.

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York

Doctors' Debate

MEDICAL TRIBUNE frequently receives extensive and well-documented communications from physicians on current subjects of controversy or those of great current medical interest. We invite contributions in these areas for presentation in this new feature.

Regarding Dr. Stern and 'Is This How a Conscience Dies?'

Below are some of the many letters responding to Dr. Arthur M. Sackler's column (MT, June 11), "Is This How a Conscience Dies?" which dealt with failure to protest the conviction and imprisonment on a charge of bribery of a Soviet physician, Dr. Mikhail Shtern, for accepting gifts of chickens and eggs from patients. Protests should be sent to Central Committee of Medical Workers, Moscow, Leninski Prospekt 42, U.S.S.R.

Correspondence from Dr. Victor Stern caused confusion about Dr. Shtern's name in Dr. Sackler's column. Victor Stern and August Stern are sons of Dr. Mikhail Shtern and it was August Stern's visit to Dr. Sackler that prompted the column.—Ed.

'Meaningless Loyalty'

Your column "Is This How A Conscience Dies?" so angered me that I won't take the time to type this letter. The delay might take the edge off my feelings.

Yes, your conscience is dead or your humanity has become buried in meaningless loyalty—i.e. to newspapers, organizations, etc. As a physician, you may at times feel that relationships between men do matter and that other constructs of social organization, governments, etc., only exist to facilitate imposition of controls necessary to prevent social chaos and perhaps the very inhumanity you refused to act against. Thus your "loyalty" and lack of conscience make a mockery out of the values you believed you were supporting.

I hope you see your hypocrisy and do some act like a sensible man rather than write a cathartic article. Your guilt won't go away.

RONALD A. BORTMAN, M.D.
Kensington, Calif.

leagues in American are deeply disturbed, and suggest that it be discussed before getting down to talking about world health man power.

The article was beautifully written and extremely moving.

DAVID PENT, M.D.
Phoenix, Ariz.

Subversion of Conscience

Your editorial regarding "death of a conscience" resulted in considerable introspection for me. It engendered feelings of overwhelming gratitude for liberty. It is so tragically easy to subvert conscience with "principle."

The "Gulag Archipelago" struck horror to my mind. The thought of all the Dr. Shterns makes one weep inside.

Please, sir, continue to stimulate our inner sensitivities. I salute your courage in using your position in such a thought-provoking and forthright fashion.

RICHARD E. CARLSON, M.D.
Kirkland, Wash.

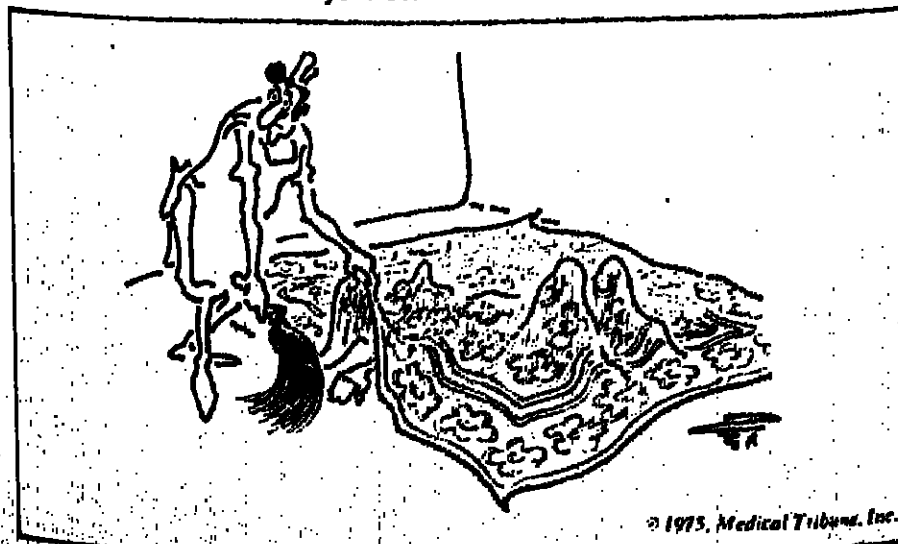
A Resounding 'Yes'

In answer to Arthur M. Sackler's question, "Is this how a conscience dies?", a resounding YES, Dr. Sackler. International Publisher, MEDICAL TRIBUNE, must have felt terribly guilty, and indeed he should have. "Uneasy" is his word to describe his weaseling, fish-tailing and generally mushy handling of the efforts of a Russian dissident scientist to get published, and of that scientist's efforts to save the life of his physician-father, imprisoned in the Soviet Union on charges that his son thought trumped up. So the policy of the MEDICAL TRIBUNE has been to avoid politics; big deal: maybe someone in the Western world appreciates

To the Central Committee...

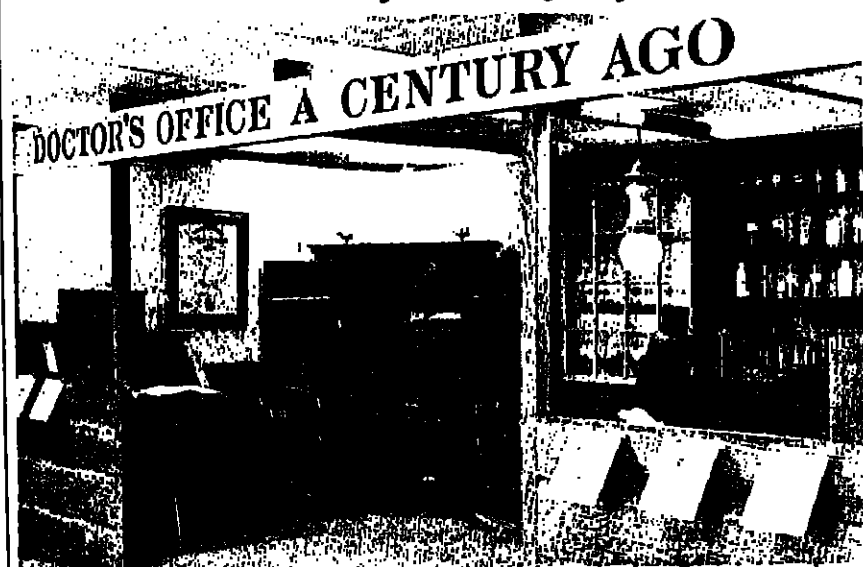
It seems to me, as I sat down to write a letter to the Central Committee of Union of Medical Workers in Leningrad, U.S.S.R., that it would have about as much effect as throwing a pail of water into the ocean. Granted, if enough pails of water were thrown in it might make a difference.

However, it seems to me that the much more effective approach to assist physicians like Dr. Stern would be to express our concerns to individuals like you, who have direct contact with health officials in Russia. Then you could make them aware that your col-



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A Gift to Academy of Family Physicians



The American Academy of Family Physicians has been given the display of a physician's office of a century ago by Mead Johnson Laboratories. The office shows instruments, books, furniture, an amputation kit, field microscope, prescription scale, a spring lancet used in bloodletting, mortars and pestles, drug jars, and an examination chair. All of the items were used by a doctor.

that concept, certainly no one in the Soviet Union does. Whatever happens in Russia is totally political. If the face that Soviet science turns to the rest of the world seems non-political it is because it serves Russia's political needs to have that appear to be so, in that manner, at that time, until it serves their needs for something else to appear to be so. "What principle?" Dr. Sackler finally asked himself, "shaken." Indeed, Doctor, what principle? I'm afraid he's confusing principle with lack of gut. When the chips were down the International Publisher didn't have anything inside. It's up to every one of us at every opportunity that presents itself to do any meaningful and useful thing to aid the efforts of Soviet dissidents to help themselves and their families. Dr. Sackler's allusion to the plight of those who suffered under the Nazi terror is well founded. Dr. Sackler's conscience is not dead yet, or he wouldn't have written his long "mea culpa," but for heaven's sake, Art, turn down the volume of von Karmann conducting Brahms' First, let some of the ego-trip fall away from your erstwhile effort to "establish a task force on world health manpower" and listen to what's going on in life today on the level of individuals struggling to free themselves from the totalitarianism of the left.

RICHARD H. POLLEN, M.D., F.A.C.P.
Kensington, Md.

'Excuse for Inaction'

I am writing to you in response to your article concerning your conscience, in which you agonized over your failure to help Dr. August Stern's father, who has been imprisoned unjustly, as you make it clear in your article. In your opinion at least, it is unjust.

It is with a great feeling of sadness that I write you. I assure you I do wish to be polite to you because I do want you to act in this matter as you should. It would be an even greater sadness if you should be repelled and fail to act. My sadness is from disappointment.

You probably intended all along to help the Sterns. You clearly state in your article that you have contacts and can do it. You appear to be proud of

of your credentials and your international accomplishments. You list some experiences and then compare yourself with those who kept quiet during the Nazi era and express admiration for those who did not. You clearly do not respect your own behavior in this matter, and wonder aloud if anyone else cares, if they have written.

Your excuse for inaction is "principle." Surely, you can't mean you find some principle for not making use of yourself. For fear of antagonizing your Publisher, on loss of Eastern bloc subscribers or some "scientific interchange"—all impersonal, theatrical reasons, you would withhold help you could give? Whenever we fail to act in such a straightforward case as this, it is usually (always?) because we put our needs first. Surely, whatever need you have is not worth a man's life.

Further, you should publish what you have done and how you felt better for having tried to help the Sterns after you have done it, as encouragement and inspiration for those readers of yours who will be influenced by your noninvolvement and feel that it's all right for the omissions of moral or ethical behavior because you have set a precedent.

So, to answer your question, there are some of us who care already. You can lead others to care by doing what you should. You show you know the difference between right and wrong. I am confident you will integrate yourself into a great endeavor and not rest until you have exhausted yourself in helping Dr. Shtern. You should hope someone would do as much for you some day. Could you find a better principle than this? I, for one, reject all those other "principles" as excuses, which I mention with patience because I know we are not always as sure of our own motives.

With best wishes for you and the Sterns, I am

TOM R. GAMBRILL, M.D.
Fullerton, Calif.

P.S. Need bibliography? Read Hochhuth's *Stilvertreter (The Deputy)*, the biography of Pope John XXIII, Schwartz-Bart's *The Last of the Mob*, Kant's *Ethical Principles*, etc., Schlipps' *Philosophy of Martin Buber*.

Aspirin Scores High As an Antiarthritic In Synovial Testing

Medical Tribune Report

NEW ORLEANS—The old standby, aspirin, gets high marks in a new system developed at the Massachusetts General Hospital for testing antiarthritic drugs.

The method reported at the American Rheumatism Association meeting here uses cultures of synovial tissue taken at surgery from the joints of rheumatoid arthritis patients.

Dr. F. G. Kantrowitz and his colleagues found that the tissues continued to produce abnormal amounts of prostaglandin E₂, believed by many investigators to be involved in inflammatory reactions associated with arthritis.

The synovial tissue, he said, is 100 to 1000 times more sensitive than the bovine seminal vesicle microsomal preparations which have been used until now to study the effectiveness of drugs in the inhibition of prostaglandin biosynthesis.

Drugs having weak effects, or none at all, included these agents now widely used in the treatment of rheumatic diseases: azathioprine, hydroxychloroquine, acetaminophen and penicillamine. Dr. Kantrowitz said sodium salicylate and gold sodium thiomalate did not produce any significant inhibition. He speculated that these drugs probably exert their major effects via other mechanisms.

Dexamethasone Very Effective

Tests with bovine seminal vesicle preparations indicate that the corticosteroids are inactive in inhibiting prostaglandin biosynthesis. But the Boston investigators found that dexamethasone, when tested with synovial tissue, showed striking inhibitory properties.

Dr. Kantrowitz said this fact eventually might prove to be the most important discovery made with synovial tissue cultures because it may be possible to isolate the part of the dexamethasone molecule which is effective and use it clinically without subjecting patients to the side effects of steroids.

He said the study does nothing to compromise the position of aspirin as the first line drug for treating rheumatoid arthritis patients. He said aspirin controls the symptoms, and can be tolerated in large amounts by most patients if taken on a full stomach or in buffered form.

He acknowledged there is controversy over the question of whether prostaglandin is inflammatory or anti-inflammatory. But he said the data are weighted on the inflammatory side, although PGE₂ seems to be anti-inflammatory.

Dr. Kantrowitz' co-worker, Dr. Dwight R. Robinson, presented another paper resulting from the synovial tissue work. He said apparently PGE₂ produced locally by synovial tissue, "may contribute to the destruction of juxta-articular bone in rheumatoid arthritis."

Dr. Lawrence Levine and Ms. Mary McGuire also were associated with Dr. Kantrowitz, and Dr. A. H. Tashjian Jr. with Dr. Robinson.

"Most moderately hypertensive patients who have remained hypertensive despite thiazide and reserpine therapy can attain an acceptable level of blood pressure with this drug [guanethidine]."

1. Langford HG: Hypertension, In Conn HF (ed): Current Therapy. Philadelphia, The WB Saunders Co, 1973, p 201.

When hypertension threatens to outrun control...

Although useful for mild to moderate hypertension, the classical thiazide-reserpine regimen often proves insufficient to control the moderate to severe hypertensive.

Substituted for reserpine, or added cautiously to a thiazide-reserpine regimen, Ismelin may well provide the extra measure of control necessary. Because guanethidine is perhaps the most effective antihypertensive ever available, Ismelin usually brings blood pressure down to stay.

And used with thiazides, which augment the antipressor activity of more potent agents, including guanethidine... the required addition may be less.

Whenever Ismelin is added to other antihypertensives, initial doses should

be small, and increased gradually by small increments. Once blood pressure control is achieved, all drug dosages should be reduced to the lowest effective level. Reduction of dosage often minimizes side effects.

Patients should be warned about the potential hazards of orthostatic hypotension, and cautioned to avoid sudden or prolonged standing or exercise.

A little extra patient cooperation may be required.

But it may well be worth it—for the extra protection Ismelin offers against uncontrolled hypertension.

Ismelin—usually effective in convenient once-a-day dosage—encourages patient compliance.

References:

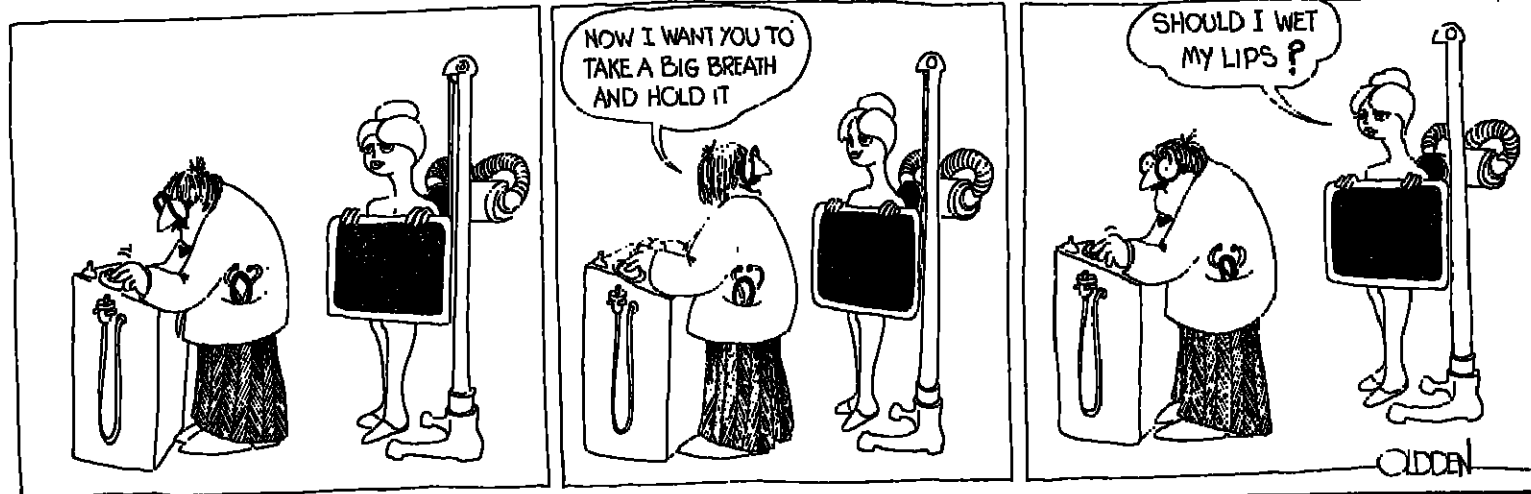
1. Langford HG: Hypertension, In Conn HF (ed): Current Therapy. Philadelphia, The WB Saunders Co, 1973, p 201.
2. Conn HF: Drugs for arterial hypertension. In Conn HF (ed): Current Therapy. Philadelphia, The WB Saunders Co, 1973, p 201.

Ismelin® sulfate
(guanethidine sulfate)
INDICATIONS: Moderate and severe hypertension either alone or as an adjunct.
CONTRAINDICATIONS: Known or suspected pheochromocytoma; hypersensitivity (rash, sensitive heart failure not due to hypertension); patients taking MAO inhibitors.
WARNINGS: Ismelin is a potent drug and can lead to disturbing and serious clinical problems. Physicians should be familiar with the details of its use before prescribing, and patients should be warned not to deviate from instructions.

Warn patients about the potential hazard of orthostatic hypotension, which can occur frequently and is most marked in the morning, and is accentuated by hot weather, alcohol, and is accompanied by lightheadedness, dizziness, or fainting. To help prevent fainting, warn patients to sit or lie down with head of bed lowered, and avoid sudden changes in posture, especially when rising from a seated or supine position. The potential occurrence of these symptoms may require alteration of these daily activities. Caution patients to avoid sudden or prolonged standing or exercise while taking the drug.

Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression.

Clinical Trials



By Olden

TRIBUNE SPORTS REPORT

X-Rays Show Neck Damage In 1 of 3 College Grid Rookies

Medical Tribune Report

IOWA CITY—A controlled study of incoming rookie players at the University of Iowa has found that one out of three showed radiologic evidence of damage to neck vertebrae at the time of his first college physical examination.

Dr. John P. Albright, Assistant Professor of Orthopedic Surgery, added that a group of students who did not play football gave no evidence of neck abnormality, he added.

As a result of the study, Dr. Albright and his colleague, Dr. Harley Feldick, director of the Student Health Service and team physician, urged "more extensive use of x-ray examination when neck pain is present, along with a delay in return to practice if there is pain or other symptom."

The "shocking" incidence of compression fractures, disk narrowing, and posterior element fractures would have been missed if only the physical exam

had been used for evaluation, they pointed out.

After studying local high-school football tactics, the investigators also recommended routine neck x-rays for high-school players.

Spearing, butting, and face-tackling, the three maneuvers held chiefly responsible for the findings, should be curtailed, they said. Spearing, in which the head is driven into a grounded offensive opponent, is already illegal, they noted, but butting and face-tackling are not.

In butting, they explained, the lowered head is used in blocking and tackling, and in face-tackling, the player aims his head at the opponent's jersey number and extends both head and neck at impact.

"Some persons think the elimination of the present-day rigid face-mask would discourage such tackling," Dr. Feldick said, but it would also increase the number of broken noses?

Orthodontic Subject



This monkey's jaw has been realigned as part of an orthodontic study at the University of Washington. The study, seeking new ways of aligning teeth by altering the structure of facial bones, is being directed by Benjamin Moffet, Ph.D., Professor of Orthodontics.

Maternal Smoking Said to Raise Perinatal Death Rate by Third

Medical Tribune Report

NEW YORK—The woman who smokes cigarettes during pregnancy is literally "smoking for two." She is not only endangering her own health, but doubles the chances of a low-birth-weight infant and increases by one-third the possibility of perinatal death.

The effects of maternal smoking on the fetus are also "dosage-related"—the more the mother smokes, the worse it is for the fetus, Dr. Neville Butler, Professor of Child Health, University of Bristol, England, told the Third World Conference on Smoking and Health, held here.

He added that, if the mother stops smoking during the first half of her pregnancy, "the baby has a 100 per cent good chance of no risks and a normal birth weight."

Just one cigarette, Dr. Butler told his audience, increases the mother's level of carboxyhemoglobin by 10 per cent, and this goes straight to the fetus, with a comparable decrease in available oxygen.

In fact, "among smokers, higher carbon monoxide levels have been

found in fetal tissues than in maternal blood. The increase in carbon monoxide lasts about seven hours," he said.

In addition, smoking two cigarettes during the last 10 weeks of pregnancy decreases fetal breathing movements by one-third, according to a study of 18 pregnancies at Oxford University. Normally, Dr. Butler said, the fetus breathes 60 per cent of the time, but after these mothers smoked only two cigarettes, the fetal movements, measured by ultrasonography, dropped to 40 per cent.

Heart Rate Rise Noted in 1935

That the fetal heart rate goes up as well after a single cigarette was reported in 1935, Dr. Butler added.

According to the British Perinatal Mortality Study, in which Dr. Butler and others studied some 13,000 children for over 11 years, the effects of maternal smoking on the child's later development are minor in individual cases, but reflect a serious problem on a mass scale, he commented.

At age 11, for example, children of mothers who smoked during pregnancy

were an average of three months behind others in reading skills and three-fourths of an inch shorter, Dr. Butler reported. Apparently then, smoking early in life, very early in life, does indeed stunt one's growth.

The mother's other children are in greater danger from respiratory illness and asthma attacks, he said.

Despite the mounting evidence against cigarettes, Dr. Butler also reported that in Great Britain, more pregnant women are smoking now than before. In 1966, he said, 36 per cent of pregnant women smoked cigarettes; by 1971, the figure was 41 per cent.

He attributed the rise to the fact that the British health education campaign against smoking has not been direct enough. "Everyone is afraid of frightening mothers," he said, citing a recent controversy over an antismoking poster, "but I think this is a risk which has to be taken."

"If we had \$200,000,000 to promote stopping the way tobacco companies have had for research and advertising in favor of smoking, I think we would have better success," he added.

IMMATERIA MEDICA

The Problem at Bunker Hill

Because Dr. Joseph Warren was one of the fallen patriotic heroes of the Battle of Bunker Hill, celebrated on a 10-cent stamp and the front page of MEDICAL TRIBUNE, we dispatched one of our footloose correspondents to the reenactment of that battle.

We won't get into why he never reported until now except to say that he came in wearing a ketchup-soaked bandage and claimed to be one of the few true survivors of the re-enactment. He asserts that the real trouble with the official reenactment wasn't the chicken-wire and papier-mache barricades that dummed in for the breastworks of 1775. Mostly, he says, the trouble came from the fact that we have better powder now and the smoke so completely obscured the battle that no one knew too much about what was happening. And the real crisis came when burly Charlie McGonagle, captain of the defending Charlestown Militia, gave the historic order, "Don't fire 'til you see the whites of their eyes," and the British Redcoats turned out to be wearing sunglasses.

So you see why the British won again, just as they did in 1775. At least, that's our man's story.

Four Before Bed

• "Six patients died before fulfilling the electroencephalographic criteria for death," notes the abstract of a J.A.M.A. article, which Dr. Hugh Haden of Birmingham, Ala., felt was rather inconsiderate of them.

• "Three women have been failed in connection with yesterday's finely timed escape," reads a New York Daily News item sent by Dr. Robert Y. Pick, of Jackson Heights, N.Y. Looks like more male chauvinism from here.

• "My roots are portable," says Anais Nin, in Vol. 5, of her diary interminable, published by Harcourt Brace Jovanovich. Meaning, of course, she is rooted in herself.

• Now that baseball's heading for the Series, we keep being haunted by Kay Iselin Gilman's characterization of Howard Cosell as "an auditory toothache." We don't even have to hear him to know what she means.